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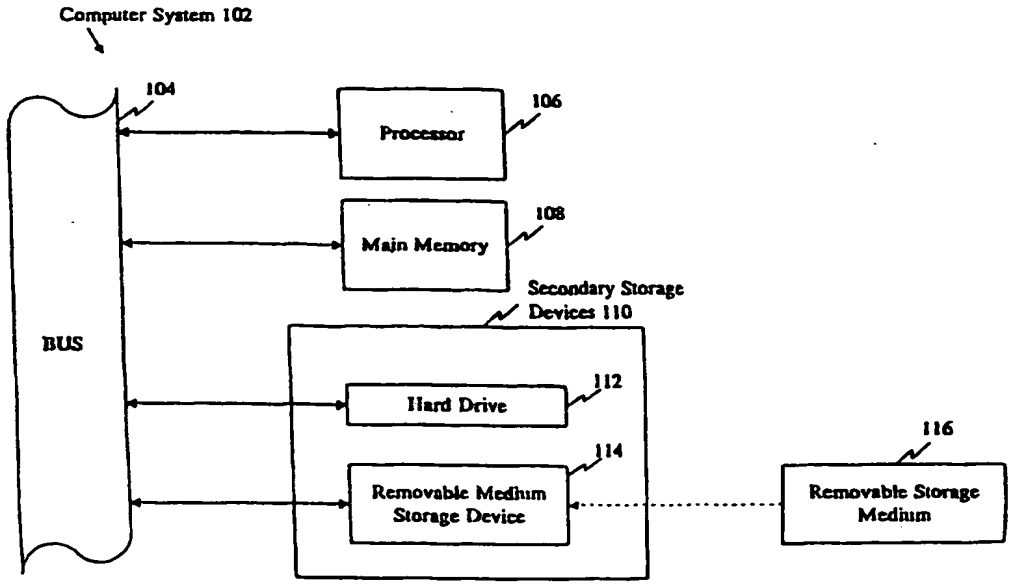

(57) Abstract

The present invention provides polynucleotide sequences of the genome of *Streptococcus pneumoniae*, polypeptide sequences encoded by the polynucleotide sequences, corresponding polynucleotides and polypeptides, vectors and hosts comprising the polynucleotides, and assays and other uses thereof. The present invention further provides polynucleotide and polypeptide sequence information stored on computer readable media, and computer–based systems and methods which facilitate its use.

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Streptococcus pneumoniae Polynucleotides and Sequences

FIELD OF THE INVENTION

The present invention relates to the field of molecular biology. In particular, it relates to, among other things, nucleotide sequences of *Streptococcus pneumoniae*, contigs, ORFs, fragments, probes, primers and related polynucleotides thereof, peptides and polypeptides encoded by the sequences, and uses of the polynucleotides and sequences thereof, such as in fermentation, polypeptide production, assays and pharmaceutical development, among others.

BACKGROUND OF THE INVENTION

Streptococcus pneumoniae has been one of the most extensively studied microorganisms since its first isolation in 1881. It was the object of many investigations that led to important scientific discoveries. In 1928, Griffith observed that when heat-killed encapsulated pneumococci and live strains constitutively lacking any capsule were concomitantly injected into mice, the nonencapsulated could be converted into encapsulated pneumococci with the same capsular type as the heat-killed strain. Years later, the nature of this "transforming principle," or carrier of genetic information, was shown to be DNA. (Avery, O.T., *et al., J. Exp. Med., 79:*137-157 (1944)).

In spite of the vast number of publications on *S. pneumoniae* many questions about its virulence are still unanswered, and this pathogen remains a major causative agent of serious human disease, especially community-acquired pneumonia. (Johnston, R.B., *et al., Rev. Infect. Dis. 13*(Suppl. 6):S509-517 (1991)). In addition, in developing countries, the pneumococcus is responsible for the death of a large number of children under the age of 5 years from pneumococcal pneumonia. The incidence of pneumococcal disease is highest in infants under 2 years of age and in people over 60 years of age. Pneumococci are the second most frequent cause (after *Haemophilus influenzae* type b) of bacterial meningitis and otitis media in children. With the recent introduction of conjugate vaccines for *H. influenzae* type b, pneumococcal meningitis is likely to become increasingly prominent. *S. pneumoniae* is the most important etiologic agent of community-

acquired pneumonia in adults and is the second most common cause of bacterial meningitis behind *Neisseria meningitidis*.

The antibiotic generally prescribed to treat *S. pneumoniae* is benzylpenicillin, although resistance to this and to other antibiotics is found occasionally. Pneumococcal resistance to penicillin results from mutations in its penicillin-binding proteins. In uncomplicated pneumococcal pneumonia caused by a sensitive strain, treatment with penicillin is usually successful unless started too late. Erythromycin or clindamycin can be used to treat pneumonia in patients hypersensitive to penicillin, but resistant strains to these drugs exist. Broad spectrum antibiotics (e.g., the tetracyclines) may also be effective, although tetracycline-resistant strains are not rare. In spite of the availability of antibiotics, the mortality of pneumococcal bacteremia in the last four decades has remained stable between 25 and 29%. (Gillespie, S.H., *et al., J. Med. Microbiol. 28*:237-248 (1989).

S. pneumoniae is carried in the upper respiratory tract by many healthy individuals. It has been suggested that attachment of pneumococci is mediated by a disaccharide receptor on fibronectin, present on human pharyngeal epithelial cells. (Anderson, B.J., *et al., J. Immunol. 142*:2464-2468 (1989). The mechanisms by which pneumococci translocate from the nasopharynx to the lung, thereby causing pneumonia, or migrate to the blood, giving rise to bacteremia or septicemia, are poorly understood. (Johnston, R.B., *et al., Rev. Infect. Dis. 13*(Suppl. 6):S509-517 (1991).

Various proteins have been suggested to be involved in the pathogenicity of *S. pneumoniae*, however, only a few of them have actually been confirmed as virulence factors. Pneumococci produce an IgA1 protease that might interfere with host defense at mucosal surfaces. (Kornfield, S.J., *et al., Rev. Inf. Dis. 3*:521-534 (1981). *S. pneumoniae* also produces neuraminidase, an enzyme that may facilitate attachment to epithelial cells by cleaving sialic acid from the host glycolipids and gangliosides. Partially purified neuraminidase was observed to induce meningitis-like symptoms in mice; however, the reliability of this finding has been questioned because the neuraminidase preparations used were probably contaminated with cell wall products. Other pneumococcal proteins besides neuraminidase are involved in the adhesion of pneumococci to epithelial and endothelial cells. These pneumococcal proteins have as yet not been identified. Recently, Cundell *et. al.*, reported that peptide permeases can modulate

pneumococcal adherence to epithelial and endothelial cells. It was, however, unclear whether these permeases function directly as adhesions or whether they enhance adherence by modulating the expression of pneumococcal adhesions. (DeVelasco, E.A., *et al.*, *Micro. Rev.* 59:591-603 (1995). A better understanding of the virulence factors determining its pathogenicity will need to be developed to cope with the devastating effects of pneumococcal disease in humans.

Ironically, despite the prominent role of *S. pneumoniae* in the discovery of DNA, little is known about the molecular genetics of the organism. The *S. pneumoniae* genome consists of one circular, covalently closed, double-stranded DNA and a collection of so-called variable accessory elements, such as prophages, plasmids, transposons and the like. Most physical characteristics and almost all of the genes of *S. pneumoniae* are unknown. Among the few that have been identified, most have not been physically mapped or characterized in detail. Only a few genes of this organism have been sequenced. (See, for instance current versions of GENBANK and other nucleic acid databases, and references that relate to the genome of *S. pneumoniae* such as those set out elsewhere herein.)

It is clear that the etiology of diseases mediated or exacerbated by *S. pneumoniae*, infection involves the programmed expression of *S. pneumoniae* genes, and that characterizing the genes and their patterns of expression would add dramatically to our understanding of the organism and its host interactions. Knowledge of *S. pneumoniae* genes and genomic organization would improve our understanding of disease etiology and lead to improved and new ways of preventing, ameliorating, arresting and reversing diseases. Moreover, characterized genes and genomic fragments of *S. pneumoniae* would provide reagents for, among other things, detecting, characterizing and controlling *S. pneumoniae* infections. There is a need to characterize the genome of *S. pneumoniae* and for polynucleotides of this organism.

SUMMARY OF THE INVENTION

The present invention is based on the sequencing of fragments of the *Streptococcus pneumoniae* genome. The primary nucleotide sequences which were generated are provided in SEQ ID NOS:1-391.

The present invention provides the nucleotide sequence of several hundred contigs of the *Streptococcus pneumoniae* genome, which are listed in tables below and set out in the Sequence Listing submitted herewith, and representative fragments thereof, in a form which can be readily used, analyzed, and interpreted by a skilled artisan. In one embodiment, the present invention is provided as contiguous strings of primary sequence information corresponding to the nucleotide sequences depicted in SEQ ID NOS:1-391.

The present invention further provides nucleotide sequences which are at least 95% identical to the nucleotide sequences of SEQ ID NOS:1-391.

The nucleotide sequence of SEQ ID NOS:1-391, a representative fragment thereof, or a nucleotide sequence which is at least 95% identical to the nucleotide sequence of SEQ ID NOS:1-391 may be provided in a variety of mediums to facilitate its use. In one application of this embodiment, the sequences of the present invention are recorded on computer readable media. Such media includes, but is not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media.

The present invention further provides systems, particularly computer-based systems which contain the sequence information herein described stored in a data storage means. Such systems are designed to identify commercially important fragments of the *Streptococcus pneumoniae* genome.

Another embodiment of the present invention is directed to fragments of the *Streptococcus pneumoniae* genome having particular structural or functional attributes. Such fragments of the *Streptococcus pneumoniae* genome of the present invention include, but are not limited to, fragments which encode peptides, hereinafter referred to as open reading frames or ORFs, fragments which modulate the expression of an operably linked ORF, hereinafter referred to as expression modulating fragments or EMFs, and fragments which can be used to diagnose the

presence of *Streptococcus pneumoniae* in a sample, hereinafter referred to as diagnostic fragments or DFs.

Each of the ORFs in fragments of the *Streptococcus pneumoniae* genome disclosed in Tables 1-3, and the EMFs found 5' to the ORFs, can be used in numerous ways as polynucleotide reagents. For instance, the sequences can be used as diagnostic probes or amplification primers for detecting or determining the presence of a specific microbe in a sample, to selectively control gene expression in a host and in the production of polypeptides, such as polypeptides encoded by ORFs of the present invention, particular those polypeptides that have a pharmacological activity.

The present invention further includes recombinant constructs comprising one or more fragments of the *Streptococcus pneumoniae* genome of the present invention. The recombinant constructs of the present invention comprise vectors, such as a plasmid or viral vector, into which a fragment of the *Streptococcus pneumoniae* has been inserted.

The present invention further provides host cells containing any of the isolated fragments of the *Streptococcus pneumoniae* genome of the present invention. The host cells can be a higher eukaryotic host cell, such as a mammalian cell, a lower eukaryotic cell, such as a yeast cell, or a procaryotic cell such as a bacterial cell.

The present invention is further directed to isolated polypeptides and proteins encoded by ORFs of the present invention. A variety of methods, well known to those of skill in the art, routinely may be utilized to obtain any of the polypeptides and proteins of the present invention. For instance, polypeptides and proteins of the present invention having relatively short, simple amino acid sequences readily can be synthesized using commercially available automated peptide synthesizers. Polypeptides and proteins of the present invention also may be purified from bacterial cells which naturally produce the protein. Yet another alternative is to purify polypeptide and proteins of the present invention from cells which have been altered to express them.

The invention further provides methods of obtaining homologs of the fragments of the *Streptococcus pneumoniae* genome of the present invention and homologs of the proteins encoded by the ORFs of the present invention. Specifically, by using the nucleotide and amino acid sequences disclosed herein as

a probe or as primers, and techniques such as PCR cloning and colony/plaque hybridization, one skilled in the art can obtain homologs.

The invention further provides antibodies which selectively bind polypeptides and proteins of the present invention. Such antibodies include both monoclonal and polyclonal antibodies.

The invention further provides hybridomas which produce the above-described antibodies. A hybridoma is an immortalized cell line which is capable of secreting a specific monoclonal antibody.

The present invention further provides methods of identifying test samples derived from cells which express one of the ORFs of the present invention, or a homolog thereof. Such methods comprise incubating a test sample with one or more of the antibodies of the present invention, or one or more of the DFs of the present invention, under conditions which allow a skilled artisan to determine if the sample contains the ORF or product produced therefrom.

In another embodiment of the present invention, kits are provided which contain the necessary reagents to carry out the above-described assays.

Specifically, the invention provides a compartmentalized kit to receive, in close confinement, one or more containers which comprises: (a) a first container comprising one of the antibodies, or one of the DFs of the present invention; and (b) one or more other containers comprising one or more of the following: wash reagents, reagents capable of detecting presence of bound antibodies or hybridized DFs.

Using the isolated proteins of the present invention, the present invention further provides methods of obtaining and identifying agents capable of binding to a polypeptide or protein encoded by one of the ORFs of the present invention. Specifically, such agents include, as further described below, antibodies, peptides, carbohydrates, pharmaceutical agents and the like. Such methods comprise steps of: (a) contacting an agent with an isolated protein encoded by one of the ORFs of the present invention; and (b) determining whether the agent binds to said protein.

The present genomic sequences of *Streptococcus pneumoniae* will be of great value to all laboratories working with this organism and for a variety of commercial purposes. Many fragments of the *Streptococcus pneumoniae* genome will be immediately identified by similarity searches against GenBank or protein databases and will be of immediate value to *Streptococcus pneumoniae* researchers

and for immediate commercial value for the production of proteins or to control gene expression.

The methodology and technology for elucidating extensive genomic sequences of bacterial and other genomes has and will greatly enhance the ability to analyze and understand chromosomal organization. In particular, sequenced contigs and genomes will provide the models for developing tools for the analysis of chromosome structure and function, including the ability to identify genes within large segments of genomic DNA, the structure, position, and spacing of regulatory elements, the identification of genes with potential industrial applications, and the ability to do comparative genomic and molecular phylogeny.

DESCRIPTION OF THE FIGURES

FIGURE 1 is a block diagram of a computer system (102) that can be used to implement computer-based systems of present invention.

FIGURE 2 is a schematic diagram depicting the data flow and computer programs used to collect, assemble, edit and annotate the contigs of the *Streptococcus pneumoniae* genome of the present invention. Both Macintosh and Unix platforms are used to handle the AB 373 and 377 sequence data files, largely as described in Kerlavage *et al.*, *Proceedings of the Twenty-Sixth Annual Hawaii International Conference on System Sciences*, 585, IEEE Computer Society Press, Washington D.C. (1993). Factura (AB) is a Macintosh program designed for automatic vector sequence removal and end-trimming of sequence files. The program Loadis runs on a Macintosh platform and parses the feature data extracted from the sequence files by Factura to the Unix based *Streptococcus pneumoniae* relational database. Assembly of contigs (and whole genome sequences) is accomplished by retrieving a specific set of sequence files and their associated features using Extrseq, a Unix utility for retrieving sequences from an SQL database. The resulting sequence file is processed by seq_filter to trim portions of the sequences with more than 2% ambiguous nucleotides. The sequence files were assembled using TIGR Assembler, an assembly engine designed at The Institute for Genomic Research (TIGR) for rapid and accurate assembly of thousands of sequence fragments. The collection of contigs generated by the assembly step is loaded into the database with the lassie program. Identification of open reading

frames (ORFs) is accomplished by processing contigs with zorf or GenMark. The ORFs are searched against *S. pneumoniae* sequences from GenBank and against all protein sequences using the BLASTN and BLASTP programs, described in Altschul *et al., J. Mol. Biol. 215:* 403-410 (1990)). Results of the ORF determination and similarity searching steps were loaded into the database. As described below, some results of the determination and the searches are set out in Tables 1-3.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

The present invention is based on the sequencing of fragments of the *Streptococcus pneumoniae* genome and analysis of the sequences. The primary nucleotide sequences generated by sequencing the fragments are provided in SEQ ID NOS:1-391. (As used herein, the "primary sequence" refers to the nucleotide sequence represented by the IUPAC nomenclature system.)

In addition to the aforementioned *Streptococcus pneumoniae* polynucleotide and polynucleotide sequences, the present invention provides the nucleotide sequences of SEQ ID NOS:1-391, or representative fragments thereof, in a form which can be readily used, analyzed, and interpreted by a skilled artisan.

As used herein, a "representative fragment of the nucleotide sequence depicted in SEQ ID NOS:1-391" refers to any portion of the SEQ ID NOS:1-391 which is not presently represented within a publicly available database. Preferred representative fragments of the present invention are *Streptococcus pneumoniae* open reading frames (ORFs), expression modulating fragment (EMFs) and fragments which can be used to diagnose the presence of *Streptococcus pneumoniae* in sample (DFs). A non-limiting identification of preferred representative fragments is provided in Tables 1-3. As discussed in detail below, the information provided in SEQ ID NOS:1-391 and in Tables 1-3 together with routine cloning, synthesis, sequencing and assay methods will enable those skilled in the art to clone and sequence all "representative fragments" of interest, including open reading frames encoding a large variety of *Streptococcus pneumoniae* proteins.

While the presently disclosed sequences of SEQ ID NOS:1-391 are highly accurate, sequencing techniques are not perfect and, in relatively rare instances, further investigation of a fragment or sequence of the invention may reveal a

nucleotide sequence error present in a nucleotide sequence disclosed in SEQ ID NOS:1-391. However, once the present invention is made available (*i.e.*, once the information in SEQ ID NOS:1-391 and Tables 1-3 has been made available), resolving a rare sequencing error in SEQ ID NOS:1-391 will be well within the skill of the art. The present disclosure makes available sufficient sequence information to allow any of the described contigs or portions thereof to be obtained readily by straightforward application of routine techniques. Further sequencing of such polynucleotide may proceed in like manner using manual and automated sequencing methods which are employed ubiquitous in the art. Nucleotide sequence editing software is publicly available. For example, Applied Biosystem's (AB) AutoAssembler can be used as an aid during visual inspection of nucleotide sequences. By employing such routine techniques potential errors readily may be identified and the correct sequence then may be ascertained by targeting further sequencing effort, also of a routine nature, to the region containing the potential error.

Even if all of the very rare sequencing errors in SEQ ID NOS:1-391 were corrected, the resulting nucleotide sequences would still be at least 95% identical, nearly all would be at least 99% identical, and the great majority would be at least 99.9% identical to the nucleotide sequences of SEQ ID NOS:1-391.

As discussed elsewhere herein, polynucleotides of the present invention readily may be obtained by routine application of well known and standard procedures for cloning and sequencing DNA. Detailed methods for obtaining libraries and for sequencing are provided below, for instance. A wide variety of *Streptococcus pneumoniae* strains that can be used to prepare *S. pneumoniae* genomic DNA for cloning and for obtaining polynucleotides of the present invention are available to the public from recognized depository institutions, such as the American Type Culture Collection (ATCC). While the present invention is enabled by the sequences and other information herein disclosed, the *S. pneumoniae* strain that provided the DNA of the present Sequence Listing, Strain 7/87 14.8.91, has been deposited in the ATCC, as a convenience to those of skill in the art. As a further convenience, a library of *S. pneumoniae* genomic DNA, derived from the same strain, also has been deposited in the ATCC. The *S. pneumoniae* strain was deposited on October 10, 1996, and was given Deposit No. 55840, and the cDNA library was deposited on October 11, 1996 and was given Deposit No. 97755. The genomic fragments in the library are 15 to 20 kb

fragments generated by partial Sau3A1 digestion and they are inserted into the BamHI site in the well-known lambda-derived vector lambda DASH II (Stratagene, La Jolla, CA). The provision of the deposits is not a waiver of any rights of the inventors or their assignees in the present subject matter.

The nucleotide sequences of the genomes from different strains of *Streptococcus pneumoniae* differ somewhat. However, the nucleotide sequences of the genomes of all *Streptococcus pneumoniae* strains will be at least 95% identical, in corresponding part, to the nucleotide sequences provided in SEQ ID NOS:1-391. Nearly all will be at least 99% identical and the great majority will be 99.9% identical.

Thus, the present invention further provides nucleotide sequences which are at least 95%, preferably 99% and most preferably 99.9% identical to the nucleotide sequences of SEQ ID NOS:1-391, in a form which can be readily used, analyzed and interpreted by the skilled artisan.

Methods for determining whether a nucleotide sequence is at least 95%, at least 99% or at least 99.9% identical to the nucleotide sequences of SEQ ID NOS:1-391 are routine and readily available to the skilled artisan. For example, the well known fasta algorithm described in Pearson and Lipman, *Proc. Natl. Acad. Sci. USA 85:* 2444 (1988) can be used to generate the percent identity of nucleotide sequences. The BLASTN program also can be used to generate an identity score of polynucleotides compared to one another.

COMPUTER RELATED EMBODIMENTS

The nucleotide sequences provided in SEQ ID NOS:1-391, a representative fragment thereof, or a nucleotide sequence at least 95%, preferably at least 99% and most preferably at least 99.9% identical to a polynucleotide sequence of SEQ ID NOS:1-391 may be "provided" in a variety of mediums to facilitate use thereof. As used herein, provided refers to a manufacture, other than an isolated nucleic acid molecule, which contains a nucleotide sequence of the present invention; *i.e.*, a nucleotide sequence provided in SEQ ID NOS:1-391, a representative fragment thereof, or a nucleotide sequence at least 95%, preferably at least 99% and most preferably at least 99.9% identical to a polynucleotide of SEQ ID NOS:1-391. Such a manufacture provides a large portion of the *Streptococcus pneumoniae* genome and parts thereof (*e.g.*, a *Streptococcus pneumoniae* open reading frame (ORF)) in a form which allows a skilled artisan to examine the manufacture using

means not directly applicable to examining the *Streptococcus pneumoniae* genome or a subset thereof as it exists in nature or in purified form.

In one application of this embodiment, a nucleotide sequence of the present invention can be recorded on computer readable media. As used herein, "computer readable media" refers to any medium which can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as CD- ROM; electrical storage media such as RAM and ROM; and hybrids of these categories, such as magnetic/optical storage media. A skilled artisan can readily appreciate how any of the presently known computer readable mediums can be used to create a manufacture comprising computer readable medium having recorded thereon a nucleotide sequence of the present invention. Likewise, it will be clear to those of skill how additional computer readable media that may be developed also can be used to create analogous manufactures having recorded thereon a nucleotide sequence of the present invention.

As used herein, "recorded" refers to a process for storing information on computer readable medium. A skilled artisan can readily adopt any of the presently know methods for recording information on computer readable medium to generate manufactures comprising the nucleotide sequence information of the present invention. A variety of data storage structures are available to a skilled artisan for creating a computer readable medium having recorded thereon a nucleotide sequence of the present invention. The choice of the data storage structure will generally be based on the means chosen to access the stored information. In addition, a variety of data processor programs and formats can be used to store the nucleotide sequence information of the present invention on computer readable medium. The sequence information can be represented in a word processing text file, formatted in commercially- available software such as WordPerfect and MicroSoft Word, or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase, Oracle, or the like. A skilled artisan can readily adapt any number of data-processor structuring formats (*e.g.*, text file or database) in order to obtain computer readable medium having recorded thereon the nucleotide sequence information of the present invention.

Computer software is publicly available which allows a skilled artisan to access sequence information provided in a computer readable medium. Thus, by providing in computer readable form the nucleotide sequences of SEQ ID NOS:1-

391, a representative fragment thereof, or a nucleotide sequence at least 95%, preferably at least 99% and most preferably at least 99.9% identical to a sequence of SEQ ID NOS:1-391 the present invention enables the skilled artisan routinely to access the provided sequence information for a wide variety of purposes.

The examples which follow demonstrate how software which implements the BLAST (Altschul *et al.*, *J. Mol. Biol. 215*:403-410 (1990)) and BLAZE (Brutlag *et al.*, *Comp. Chem. 17*:203-207 (1993)) search algorithms on a Sybase system was used to identify open reading frames (ORFs) within the *Streptococcus pneumoniae* genome which contain homology to ORFs or proteins from both *Streptococcus pneumoniae* and from other organisms. Among the ORFs discussed herein are protein encoding fragments of the *Streptococcus pneumoniae* genome useful in producing commercially important proteins, such as enzymes used in fermentation reactions and in the production of commercially useful metabolites.

The present invention further provides systems, particularly computer-based systems, which contain the sequence information described herein. Such systems are designed to identify, among other things, commercially important fragments of the *Streptococcus pneumoniae* genome.

As used herein, "a computer-based system" refers to the hardware means, software means, and data storage means used to analyze the nucleotide sequence information of the present invention. The minimum hardware means of the computer-based systems of the present invention comprises a central processing unit (CPU), input means, output means, and data storage means. A skilled artisan can readily appreciate that any one of the currently available computer-based systems are suitable for use in the present invention.

As stated above, the computer-based systems of the present invention comprise a data storage means having stored therein a nucleotide sequence of the present invention and the necessary hardware means and software means for supporting and implementing a search means.

As used herein, "data storage means" refers to memory which can store nucleotide sequence information of the present invention, or a memory access means which can access manufactures having recorded thereon the nucleotide sequence information of the present invention.

As used herein, "search means" refers to one or more programs which are implemented on the computer-based system to compare a target sequence or target structural motif with the sequence information stored within the data storage

means. Search means are used to identify fragments or regions of the present genomic sequences which match a particular target sequence or target motif. A variety of known algorithms are disclosed publicly and a variety of commercially available software for conducting search means are and can be used in the computer-based systems of the present invention. Examples of such software includes, but is not limited to, MacPattern (EMBL), BLASTN and BLASTX (NCBIA). A skilled artisan can readily recognize that any one of the available algorithms or implementing software packages for conducting homology searches can be adapted for use in the present computer-based systems.

As used herein, a "target sequence" can be any DNA or amino acid sequence of six or more nucleotides or two or more amino acids. A skilled artisan can readily recognize that the longer a target sequence is, the less likely a target sequence will be present as a random occurrence in the database. The most preferred sequence length of a target sequence is from about 10 to 100 amino acids or from about 30 to 300 nucleotide residues. However, it is well recognized that searches for commercially important fragments, such as sequence fragments involved in gene expression and protein processing, may be of shorter length.

As used herein, "a target structural motif," or "target motif," refers to any rationally selected sequence or combination of sequences in which the sequence(s) are chosen based on a three-dimensional configuration which is formed upon the folding of the target motif. There are a variety of target motifs known in the art. Protein target motifs include, but are not limited to, enzymic active sites and signal sequences. Nucleic acid target motifs include, but are not limited to, promoter sequences, hairpin structures and inducible expression elements (protein binding sequences).

A variety of structural formats for the input and output means can be used to input and output the information in the computer-based systems of the present invention. A preferred format for an output means ranks fragments of the *Streptococcus pneumoniae* genomic sequences possessing varying degrees of homology to the target sequence or target motif. Such presentation provides a skilled artisan with a ranking of sequences which contain various amounts of the target sequence or target motif and identifies the degree of homology contained in the identified fragment.

A variety of comparing means can be used to compare a target sequence or target motif with the data storage means to identify sequence fragments of the

Streptococcus pneumoniae genome. In the present examples, implementing software which implement the BLAST and BLAZE algorithms, described in Altschul *et al., J. Mol. Biol. 215:* 403-410 (1990), is used to identify open reading frames within the *Streptococcus pneumoniae* genome. A skilled artisan can readily recognize that any one of the publicly available homology search programs can be used as the search means for the computer-based systems of the present invention. Of course, suitable proprietary systems that may be known to those of skill also may be employed in this regard.

Figure 1 provides a block diagram of a computer system illustrative of embodiments of this aspect of present invention. The computer system 102 includes a processor 106 connected to a bus 104. Also connected to the bus 104 are a main memory 108 (preferably implemented as random access memory, RAM) and a variety of secondary storage devices 110, such as a hard drive 112 and a removable medium storage device 114. The removable medium storage device 114 may represent, for example, a floppy disk drive, a CD-ROM drive, a magnetic tape drive, *etc.* A removable storage medium 116 (such as a floppy disk, a compact disk, a magnetic tape, *etc.*) containing control logic and/or data recorded therein may be inserted into the removable medium storage device 114. The computer system 102 includes appropriate software for reading the control logic and/or the data from the removable medium storage device 114, once it is inserted into the removable medium storage device 114.

A nucleotide sequence of the present invention may be stored in a well known manner in the main memory 108, any of the secondary storage devices 110, and/or a removable storage medium 116. During execution, software for accessing and processing the genomic sequence (such as search tools, comparing tools, *etc.*) reside in main memory 108, in accordance with the requirements and operating parameters of the operating system, the hardware system and the software program or programs.

BIOCHEMICAL EMBODIMENTS

Other embodiments of the present invention are directed to isolated fragments of the *Streptococcus pneumoniae* genome. The fragments of the *Streptococcus pneumoniae* genome of the present invention include, but are not limited to fragments which encode peptides and polypeptides, hereinafter open reading frames (ORFs), fragments which modulate the expression of an operably linked ORF, hereinafter expression modulating fragments (EMFs) and fragments which can be used to diagnose the presence of *Streptococcus pneumoniae* in a sample, hereinafter diagnostic fragments (DFs).

As used herein, an "isolated nucleic acid molecule" or an "isolated fragment of the *Streptococcus pneumoniae* genome" refers to a nucleic acid molecule possessing a specific nucleotide sequence which has been subjected to purification means to reduce, from the composition, the number of compounds which are normally associated with the composition. Particularly, the term refers to the nucleic acid molecules having the sequences set out in SEQ ID NOS:1-391, to representative fragments thereof as described above, to polynucleotides at least 95%, preferably at least 99% and especially preferably at least 99.9% identical in sequence thereto, also as set out above.

A variety of purification means can be used to generate the isolated fragments of the present invention. These include, but are not limited to methods which separate constituents of a solution based on charge, solubility, or size.

In one embodiment, *Streptococcus pneumoniae* DNA can be enzymatically sheared to produce fragments of 15-20 kb in length. These fragments can then be used to generate a *Streptococcus pneumoniae* library by inserting them into lambda clones as described in the Examples below. Primers flanking, for example, an ORF, such as those enumerated in Tables 1-3 can then be generated using nucleotide sequence information provided in SEQ ID NOS:1-391. Well known and routine techniques of PCR cloning then can be used to isolate the ORF from the lambda DNA library or *Streptococcus pneumoniae* genomic DNA. Thus, given the availability of SEQ ID NOS:1-391, the information in Tables 1, 2 and 3, and the information that may be obtained readily by analysis of the sequences of SEQ ID NOS:1-391 using methods set out above, those of skill will be enabled by the present disclosure to isolate any ORF-containing or other nucleic acid fragment of the present invention.

The isolated nucleic acid molecules of the present invention include, but are not limited to single stranded and double stranded DNA, and single stranded RNA.

As used herein, an "open reading frame," ORF, means a series of triplets coding for amino acids without any termination codons and is a sequence translatable into protein.

Tables 1, 2, and 3 list ORFs in the *Streptococcus pneumoniae* genomic contigs of the present invention that were identified as putative coding regions by the GeneMark software using organism-specific second-order Markov probability transition matrices. It will be appreciated that other criteria can be used, in accordance with well known analytical methods, such as those discussed herein, to generate more inclusive, more restrictive, or more selective lists.

Table 1 sets out ORFs in the *Streptococcus pneumoniae* contigs of the present invention that over a continuous region of at least 50 bases are 95% or more identical (by BLAST analysis) to a nucleotide sequence available through GenBank in October, 1997.

Table 2 sets out ORFs in the *Streptococcus pneumoniae* contigs of the present invention that are not in Table 1 and match, with a BLASTP probability score of 0.01 or less, a polypeptide sequence available through GenBank in October, 1997.

Table 3 sets out ORFs in the *Streptococcus pneumoniae* contigs of the present invention that do not match significantly, by BLASTP analysis, a polypeptide sequence available through GenBank in October, 1997.

In each table, the first and second columns identify the ORF by, respectively, contig number and ORF number within the contig; the third column indicates the first nucleotide of the ORF (actually the first nucleotide of the stop codon immediately preceeding the ORF), counting from the 5' end of the contig strand; and the fourth column, "stop (nt)" indicates the last nucleotide of the stop codon defining the 3'end of the ORF.

In Tables 1 and 2, column five, lists the Reference for the closest matching sequence available through GenBank. These reference numbers are the databases entry numbers commonly used by those of skill in the art, who will be familiar with their denominators. Descriptions of the nomenclature are available from the National Center for Biotechnology Information. Column six in Tables 1 and 2 provides the gene name of the matching sequence; column seven provides the BLAST identity score and column eight the BLAST similarity score from the

comparison of the ORF and the homologous gene; and column nine indicates the length in nucleotides of the highest scoring segment pair identified by the BLAST identity analysis.

Each ORF described in the tables is defined by "start (nt)" (5') and "stop (nt)" (3') nucleotide position numbers. These position numbers refer to the boundaries of each ORF and provide orientation with respect to whether the forward or reverse strand is the coding strand and which reading frame the coding sequence is contained. The "start" position is the first nucleotide of the triplet encoding a stop codon just 5' to the ORF and the "stop" position is the last nucleotide of the triplet encoding the next in-frame stop codon (i.e., the stop codon at the 3' end of the ORF). Those of ordinary skill in the art appreciate that preferred fragments within each ORF described in the table include fragments of each ORF which include the entire sequence from the delineated "start" and "stop" positions excepting the first and last three nucleotides since these encode stop codons. Thus, polynucleotides set out as ORFs in the tables but lacking the three (3) 5' nucleotides and the three (3) 3' nucleotides are encompassed by the present invention. Those of skill also appreciate that particularly preferred are fragments within each ORF that are polynucleotide fragments comprising polypeptide coding sequence. As defined herein, "coding sequence" includes the fragment within an ORF beginning at the first in-frame ATG (triplet encoding methionine) and ending with the last nucleotide prior to the triplet encoding the 3' stop codon. Preferred are fragments comprising the entire coding sequence and fragments comprising the entire coding sequence, excepting the coding sequence for the N-terminal methionine. Those of skill appreciate that the N-terminal methionine is often removed during post-translational processing and that polynucleotides lacking the ATG can be used to facilitate production of N-termainal fusion proteins which may be benefical in the production or use of genetically engineered proteins. Of course, due to the degeneracy of the genetic code many polynucleotides can encode a given polypeptide. Thus, the invention further includes polynucleotides comprising a nucleotide sequence encoding a polypeptide sequence itself encoded by the coding sequence within an ORF described in Tables 1-3 herein. Further, polynucleotides at least 95%, preferably at least 99% and especially preferably at least 99.9% identical in sequence to the foregoing polynucleotides, are contemplated by the present invention.

Polypeptides encoded by polynucleotides described above and elsewhere herein are also provided by the present invention as are polypeptide comprising a an amino acid sequence at least about 95%, preferably at least 97% and even more preferably 99% identical to the amino acid sequence of a polypeptide encoded by an ORF shown in Tables 1-3. These polypeptides may or may not comprise an N-terminal methionine.

The concepts of percent identity and percent similarity of two polypeptide sequences is well understood in the art. For example, two polypeptides 10 amino acids in length which differ at three amino acid positions (*e.g.*, at positions 1, 3 and 5) are said to have a percent identity of 70%. However, the same two polypeptides would be deemed to have a percent similarity of 80% if, for example at position 5, the amino acids moieties, although not identical, were "similar" (*i.e.*, possessed similar biochemical characteristics). Many programs for analysis of nucleotide or amino acid sequence similarity, such as fasta and BLAST specifically list percent identity of a matching region as an output parameter. Thus, for instance, Tables 1 and 2 herein enumerate the percent identity of the highest scoring segment pair in each ORF and its listed relative. Further details concerning the algorithms and criteria used for homology searches are provided below and are described in the pertinent literature highlighted by the citations provided below.

It will be appreciated that other criteria can be used to generate more inclusive and more exclusive listings of the types set out in the tables. As those of skill will appreciate, narrow and broad searches both are useful. Thus, a skilled artisan can readily identify ORFs in contigs of the *Streptococcus pneumoniae* genome other than those listed in Tables 1-3, such as ORFs which are overlapping or encoded by the opposite strand of an identified ORF in addition to those ascertainable using the computer-based systems of the present invention.

As used herein, an "expression modulating fragment," EMF, means a series of nucleotide molecules which modulates the expression of an operably linked ORF or EMF.

As used herein, a sequence is said to "modulate the expression of an operably linked sequence" when the expression of the sequence is altered by the presence of the EMF. EMFs include, but are not limited to, promoters, and promoter modulating sequences (inducible elements). One class of EMFs are fragments which induce the expression or an operably linked ORF in response to a specific regulatory factor or physiological event.

EMF sequences can be identified within the contigs of the *Streptococcus pneumoniae* genome by their proximity to the ORFs provided in Tables 1-3. An intergenic segment, or a fragment of the intergenic segment, from about 10 to 200 nucleotides in length, taken from any one of the ORFs of Tables 1-3 will modulate the expression of an operably linked ORF in a fashion similar to that found with the naturally linked ORF sequence. As used herein, an "intergenic segment" refers to fragments of the *Streptococcus pneumoniae* genome which are between two ORF(s) herein described. EMFs also can be identified using known EMFs as a target sequence or target motif in the computer-based systems of the present invention. Further, the two methods can be combined and used together.

The presence and activity of an EMF can be confirmed using an EMF trap vector. An EMF trap vector contains a cloning site linked to a marker sequence. A marker sequence encodes an identifiable phenotype, such as antibiotic resistance or a complementing nutrition auxotrophic factor, which can be identified or assayed when the EMF trap vector is placed within an appropriate host under appropriate conditions. As described above, a EMF will modulate the expression of an operably linked marker sequence. A more detailed discussion of various marker sequences is provided below. A sequence which is suspected as being an EMF is cloned in all three reading frames in one or more restriction sites upstream from the marker sequence in the EMF trap vector. The vector is then transformed into an appropriate host using known procedures and the phenotype of the transformed host in examined under appropriate conditions. As described above, an EMF will modulate the expression of an operably linked marker sequence.

As used herein, a "diagnostic fragment," DF, means a series of nucleotide molecules which selectively hybridize to *Streptococcus pneumoniae* sequences. DFs can be readily identified by identifying unique sequences within contigs of the *Streptococcus pneumoniae* genome, such as by using well-known computer analysis software, and by generating and testing probes or amplification primers

consisting of the DF sequence in an appropriate diagnostic format which determines amplification or hybridization selectivity.

The sequences falling within the scope of the present invention are not limited to the specific sequences herein described, but also include allelic and species variations thereof. Allelic and species variations can be routinely determined by comparing the sequences provided in SEQ ID NOS:1-391, a representative fragment thereof, or a nucleotide sequence at least 95%, preferrably at least 99% and most at least preferably 99.9% identical to SEQ ID NOS:1-391, with a sequence from another isolate of the same species. Furthermore, to accommodate codon variability, the invention includes nucleic acid molecules coding for the same amino acid sequences as do the specific ORFs disclosed herein. In other words, in the coding region of an ORF, substitution of one codon for another which encodes the same amino acid is expressly contemplated. Any specific sequence disclosed herein can be readily screened for errors by resequencing a particular fragment, such as an ORF, in both directions (*i.e.*, sequence both strands). Alternatively, error screening can be performed by sequencing corresponding polynucleotides of *Streptococcus pneumoniae* origin isolated by using part or all of the fragments in question as a probe or primer.

Preferred DFs of the present invention comprise at least about 17, preferrably at least about 20, and more preferrably at least about 50 contiguous nucleotides within an ORF set out in Tables 1-3. Most highly preferred DFs specifically hybridize to a polynucleotide containing the sequence of the ORF from which they are derived. Specific hybridization occurs even under stringent conditions defined elsewhere herein.

Each of the ORFs of the *Streptococcus pneumoniae* genome disclosed in Tables 1, 2 and 3, and the EMFs found 5' to the ORFs, can be used as polynucleotide reagents in numerous ways. For example, the sequences can be used as diagnostic probes or diagnostic amplification primers to detect the presence of a specific microbe in a sample, particularly *Streptococcus pneumoniae*. Especially preferred in this regard are ORFs such as those of Table 3, which do not match previously characterized sequences from other organisms and thus are most likely to be highly selective for *Streptococcus pneumoniae*. Also particularly preferred are ORFs that can be used to distinguish between strains of *Streptococcus pneumoniae*, particularly those that distinguish medically important strain, such as drug-resistant strains.

In addition, the fragments of the present invention, as broadly described, can be used to control gene expression through triple helix formation or antisense DNA or RNA, both of which methods are based on the binding of a polynucleotide sequence to DNA or RNA. Triple helix-formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Information from the sequences of the present invention can be used to design antisense and triple helix-forming oligonucleotides. Polynucleotides suitable for use in these methods are usually 20 to 40 bases in length and are designed to be complementary to a region of the gene involved in transcription, for triple-helix formation, or to the mRNA itself, for antisense inhibition. Both techniques have been demonstrated to be effective in model systems, and the requisite techniques are well known and involve routine procedures. Triple helix techniques are discussed in, for example, Lee *et al.*, *Nucl. Acids Res.* 6:3073 (1979); Cooney *et al.*, *Science* 241:456 (1988); and Dervan *et al.*, *Science* 251:1360 (1991). Antisense techniques in general are discussed in, for instance, Okano, *J. Neurochem.* 56:560 (1991) and *Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression*, CRC Press, Boca Raton, FL (1988)).

The present invention further provides recombinant constructs comprising one or more fragments of the *Streptococcus pneumoniae* genomic fragments and contigs of the present invention. Certain preferred recombinant constructs of the present invention comprise a vector, such as a plasmid or viral vector, into which a fragment of the *Streptococcus pneumoniae* genome has been inserted, in a forward or reverse orientation. In the case of a vector comprising one of the ORFs of the present invention, the vector may further comprise regulatory sequences, including, for example, a promoter, operably linked to the ORF. For vectors comprising the EMFs of the present invention, the vector may further comprise a marker sequence or heterologous ORF operably linked to the EMF.

Large numbers of suitable vectors and promoters are known to those of skill in the art and are commercially available for generating the recombinant constructs of the present invention. The following vectors are provided by way of example. Useful bacterial vectors include phagescript, PsiX174, pBluescript SK, pBS KS, pNH8a, pNH16a, pNH18a, pNH46a (available from Stratagene); pTrc99A, pKK223-3, pKK233-3, pDR540, pRIT5 (available from Pharmacia). Useful eukaryotic vectors include pWLneo, pSV2cat, pOG44, pXT1, pSG

(available from Stratagene) pSVK3, pBPV, pMSG, pSVL (available from Pharmacia).

Promoter regions can be selected from any desired gene using CAT (chloramphenicol transferase) vectors or other vectors with selectable markers. Two appropriate vectors are pKK232-8 and pCM7. Particular named bacterial promoters include lacI, lacZ, T3, T7, gpt, lambda PR, and trc. Eukaryotic promoters include CMV immediate early, HSV thymidine kinase, early and late SV40, LTRs from retrovirus, and mouse metallothionein- I. Selection of the appropriate vector and promoter is well within the level of ordinary skill in the art.

The present invention further provides host cells containing any one of the isolated fragments of the *Streptococcus pneumoniae* genomic fragments and contigs of the present invention, wherein the fragment has been introduced into the host cell using known methods. The host cell can be a higher eukaryotic host cell, such as a mammalian cell, a lower eukaryotic host cell, such as a yeast cell, or a procaryotic cell, such as a bacterial cell.

A polynucleotide of the present invention, such as a recombinant construct comprising an ORF of the present invention, may be introduced into the host by a variety of well established techniques that are standard in the art, such as calcium phosphate transfection, DEAE, dextran mediated transfection and electroporation, which are described in, for instance, Davis, L. *et al.*, BASIC METHODS IN MOLECULAR BIOLOGY (1986).

A host cell containing one of the fragments of the *Streptococcus pneumoniae* genomic fragments and contigs of the present invention, can be used in conventional manners to produce the gene product encoded by the isolated fragment (in the case of an ORF) or can be used to produce a heterologous protein under the control of the EMF. The present invention further provides isolated polypeptides encoded by the nucleic acid fragments of the present invention or by degenerate variants of the nucleic acid fragments of the present invention. By "degenerate variant" is intended nucleotide fragments which differ from a nucleic acid fragment of the present invention (*e.g.*, an ORF) by nucleotide sequence but, due to the degeneracy of the Genetic Code, encode an identical polypeptide sequence.

Preferred nucleic acid fragments of the present invention are the ORFs and subfragments thereof depicted in Tables 2 and 3 which encode proteins.

A variety of methodologies known in the art can be utilized to obtain any one of the isolated polypeptides or proteins of the present invention. At the simplest level, the amino acid sequence can be synthesized using commercially available peptide synthesizers. This is particularly useful in producing small peptides and fragments of larger polypeptides. Such short fragments as may be obtained most readily by synthesis are useful, for example, in generating antibodies against the native polypeptide, as discussed further below.

In an alternative method, the polypeptide or protein is purified from bacterial cells which naturally produce the polypeptide or protein. One skilled in the art can readily employ well-known methods for isolating polypeptides and proteins to isolate and purify polypeptides or proteins of the present invention produced naturally by a bacterial strain, or by other methods. Methods for isolation and purification that can be employed in this regard include, but are not limited to, immunochromatography, HPLC, size-exclusion chromatography, ion-exchange chromatography, and immuno-affinity chromatography.

The polypeptides and proteins of the present invention also can be purified from cells which have been altered to express the desired polypeptide or protein. As used herein, a cell is said to be altered to express a desired polypeptide or protein when the cell, through genetic manipulation, is made to produce a polypeptide or protein which it normally does not produce or which the cell normally produces at a lower level. Those skilled in the art can readily adapt procedures for introducing and expressing either recombinant or synthetic sequences into eukaryotic or prokaryotic cells in order to generate a cell which produces one of the polypeptides or proteins of the present invention.

Any host/vector system can be used to express one or more of the ORFs of the present invention. These include, but are not limited to, eukaryotic hosts such as HeLa cells, CV-1 cell, COS cells, and Sf9 cells, as well as prokaryotic host such as *E. coli* and *B. subtilis*. The most preferred cells are those which do not normally express the particular polypeptide or protein or which expresses the polypeptide or protein at low natural level.

"Recombinant," as used herein, means that a polypeptide or protein is derived from recombinant (*e.g.*, microbial or mammalian) expression systems. "Microbial" refers to recombinant polypeptides or proteins made in bacterial or fungal (*e.g.*, yeast) expression systems. As a product, "recombinant microbial"defines a polypeptide or protein essentially free of native endogenous substances and unaccompanied by associated native glycosylation. Polypeptides or proteins expressed in most bacterial cultures, *e.g.*, *E. coli*, will be free of glycosylation modifications; polypeptides or proteins expressed in yeast will have a glycosylation pattern different from that expressed in mammalian cells.

"Nucleotide sequence" refers to a heteropolymer of deoxyribonucleotides. Generally, DNA segments encoding the polypeptides and proteins provided by this invention are assembled from fragments of the *Streptococcus pneumoniae* genome and short oligonucleotide linkers, or from a series of oligonucleotides, to provide a synthetic gene which is capable of being expressed in a recombinant transcriptional unit comprising regulatory elements derived from a microbial or viral operon.

Recombinant expression vehicle or vector" refers to a plasmid or phage or virus or vector, for expressing a polypeptide from a DNA (RNA) sequence. The expression vehicle can comprise a transcriptional unit comprising an assembly of (1) a genetic regulatory elements necessary for gene expression in the host, including elements required to initiate and maintain transcription at a level sufficient for suitable expression of the desired polypeptide, including, for example, promoters and, where necessary, an enhancer and a polyadenylation signal; (2) a structural or coding sequence which is transcribed into mRNA and translated into protein, and (3) appropriate signals to initiate translation at the beginning of the desired coding region and terminate translation at its end. Structural units intended for use in yeast or eukaryotic expression systems preferably include a leader sequence enabling extracellular secretion of translated protein by a host cell. Alternatively, where recombinant protein is expressed without a leader or transport sequence, it may include an N-terminal methionine residue. This residue may or may not be subsequently cleaved from the expressed recombinant protein to provide a final product.

"Recombinant expression system" means host cells which have stably integrated a recombinant transcriptional unit into chromosomal DNA or carry the recombinant transcriptional unit extra chromosomally. The cells can be prokaryotic or eukaryotic. Recombinant expression systems as defined herein will express

heterologous polypeptides or proteins upon induction of the regulatory elements linked to the DNA segment or synthetic gene to be expressed.

Mature proteins can be expressed in mammalian cells, yeast, bacteria, or other cells under the control of appropriate promoters. Cell-free translation systems can also be employed to produce such proteins using RNAs derived from the DNA constructs of the present invention. Appropriate cloning and expression vectors for use with prokaryotic and eukaryotic hosts are described in Sambrook *et al.*, *Molecular Cloning*: *A Laboratory Manual*, 2nd Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York (1989), the disclosure of which is hereby incorporated by reference in its entirety.

Generally, recombinant expression vectors will include origins of replication and selectable markers permitting transformation of the host cell, *e.g.*, the ampicillin resistance gene of *E. coli* and *S. cerevisiae* TRP1 gene, and a promoter derived from a highly expressed gene to direct transcription of a downstream structural sequence. Such promoters can be derived from operons encoding glycolytic enzymes such as 3- phosphoglycerate kinase (PGK), alpha-factor, acid phosphatase, or heat shock proteins, among others. The heterologous structural sequence is assembled in appropriate phase with translation initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of translated protein into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an N-terminal identification peptide imparting desired characteristics, e.g., stabilization or simplified purification of expressed recombinant product.

Useful expression vectors for bacterial use are constructed by inserting a structural DNA sequence encoding a desired protein together with suitable translation initiation and termination signals in operable reading phase with a functional promoter. The vector will comprise one or more phenotypic selectable markers and an origin of replication to ensure maintenance of the vector and, when desirable, provide amplification within the host.

Suitable prokaryotic hosts for transformation include strains of *E. coli*, *B. subtilis*, *Salmonella typhimurium* and various species within the genera *Pseudomonas* and *Streptomyces*. Others may, also be employed as a matter of choice.

As a representative but non-limiting example, useful expression vectors for bacterial use can comprise a selectable marker and bacterial origin of replication

derived from commercially available plasmids comprising genetic elements of the well known cloning vector pBR322 (ATCC 37017). Such commercial vectors include, for example, pKK223-3 (available form Pharmacia Fine Chemicals, Uppsala, Sweden) and GEM 1 (available from Promega Biotec, Madison, WI, USA). These pBR322 "backbone" sections are combined with an appropriate promoter and the structural sequence to be expressed.

Following transformation of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter, where it is inducible, is derepressed or induced by appropriate means (*e.g.*, temperature shift or chemical induction) and cells are cultured for an additional period to provide for expression of the induced gene product. Thereafter cells are typically harvested, generally by centrifugation, disrupted to release expressed protein, generally by physical or chemical means, and the resulting crude extract is retained for further purification.

Various mammalian cell culture systems can also be employed to express recombinant protein. Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts, described in Gluzman, *Cell 23:*175 (1981), and other cell lines capable of expressing a compatible vector, for example, the C127, 3T3, CHO, HeLa and BHK cell lines.

Mammalian expression vectors will comprise an origin of replication, a suitable promoter and enhancer, and also any necessary ribosome binding sites, polyadenylation site, splice donor and acceptor sites, transcriptional termination sequences, and 5' flanking nontranscribed sequences. DNA sequences derived from the SV40 viral genome, for example, SV40 origin, early promoter, enhancer, splice, and polyadenylation sites may be used to provide the required nontranscribed genetic elements.

Recombinant polypeptides and proteins produced in bacterial culture is usually isolated by initial extraction from cell pellets, followed by one or more salting-out, aqueous ion exchange or size exclusion chromatography steps. Microbial cells employed in expression of proteins can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents. Protein refolding steps can be used, as necessary, in completing configuration of the mature protein. Finally, high performance liquid chromatography (HPLC) can be employed for final purification steps.

The present invention further includes isolated polypeptides, proteins and nucleic acid molecules which are substantially equivalent to those herein described. As used herein, substantially equivalent can refer both to nucleic acid and amino acid sequences, for example a mutant sequence, that varies from a reference sequence by one or more substitutions, deletions, or additions, the net effect of which does not result in an adverse functional dissimilarity between reference and subject sequences. For purposes of the present invention, sequences having equivalent biological activity, and equivalent expression characteristics are considered substantially equivalent. For purposes of determining equivalence, truncation of the mature sequence should be disregarded.

The invention further provides methods of obtaining homologs from other strains of *Streptococcus pneumoniae*, of the fragments of the *Streptococcus pneumoniae* genome of the present invention and homologs of the proteins encoded by the ORFs of the present invention. As used herein, a sequence or protein of *Streptococcus pneumoniae* is defined as a homolog of a fragment of the *Streptococcus pneumoniae* fragments or contigs or a protein encoded by one of the ORFs of the present invention, if it shares significant homology to one of the fragments of the *Streptococcus pneumoniae* genome of the present invention or a protein encoded by one of the ORFs of the present invention. Specifically, by using the sequence disclosed herein as a probe or as primers, and techniques such as PCR cloning and colony/plaque hybridization, one skilled in the art can obtain homologs.

As used herein, two nucleic acid molecules or proteins are said to "share significant homology" if the two contain regions which possess greater than 85% sequence (amino acid or nucleic acid) homology. Preferred homologs in this regard are those with more than 90% homology. Especially preferred are those with 93% or more homology. Among especially preferred homologs those with 95% or more homology are particularly preferred. Very particularly preferred among these are those with 97% and even more particularly preferred among those are homologs with 99% or more homology. The most preferred homologs among these are those with 99.9% homology or more. It will be understood that, among measures of homology, identity is particularly preferred in this regard.

Region specific primers or probes derived from the nucleotide sequence provided in SEQ ID NOS:1-391 or from a nucleotide sequence at least 95%, particularly at least 99%, especially at least 99.5% identical to a sequence of SEQ

ID NOS:1-391 can be used to prime DNA synthesis and PCR amplification, as well as to identify colonies containing cloned DNA encoding a homolog. Methods suitable to this aspect of the present invention are well known and have been described in great detail in many publications such as, for example, Innis *et al.*, *PCR Protocols*, Academic Press, San Diego, CA (1990)).

When using primers derived from SEQ ID NOS:1-391 or from a nucleotide sequence having an aforementioned identity to a sequence of SEQ ID NOS:1-391, one skilled in the art will recognize that by employing high stringency conditions (*e.g.*, annealing at 50-60°C in 6X SSPC and 50% formamide, and washing at 50-65°C in 0.5X SSPC) only sequences which are greater than 75% homologous to the primer will be amplified. By employing lower stringency conditions (*e.g.*, hybridizing at 35-37°C in 5X SSPC and 40-45% formamide, and washing at 42°C in 0.5X SSPC), sequences which are greater than 40-50% homologous to the primer will also be amplified.

When using DNA probes derived from SEQ ID NOS:1-391, or from a nucleotide sequence having an aforementioned identity to a sequence of SEQ ID NOS:1-391, for colony/plaque hybridization, one skilled in the art will recognize that by employing high stringency conditions (*e.g.*, hybridizing at 50- 65°C in 5X SSPC and 50% formamide, and washing at 50- 65°C in 0.5X SSPC), sequences having regions which are greater than 90% homologous to the probe can be obtained, and that by employing lower stringency conditions (*e.g.*, hybridizing at 35-37°C in 5X SSPC and 40-45% formamide, and washing at 42°C in 0.5X SSPC), sequences having regions which are greater than 35-45% homologous to the probe will be obtained.

Any organism can be used as the source for homologs of the present invention so long as the organism naturally expresses such a protein or contains genes encoding the same. The most preferred organism for isolating homologs are bacteria which are closely related to *Streptococcus pneumoniae*.

ILLUSTRATIVE USES OF COMPOSITIONS OF THE INVENTION

Each ORF provided in Tables 1 and 2 is identified with a function by homology to a known gene or polypeptide. As a result, one skilled in the art can use the polypeptides of the present invention for commercial, therapeutic and industrial purposes consistent with the type of putative identification of the

polypeptide. Such identifications permit one skilled in the art to use the *Streptococcus pneumoniae* ORFs in a manner similar to the known type of sequences for which the identification is made; for example, to ferment a particular sugar source or to produce a particular metabolite. A variety of reviews illustrative of this aspect of the invention are available, including the following reviews on the industrial use of enzymes, for example, BIOCHEMICAL ENGINEERING AND BIOTECHNOLOGY HANDBOOK, 2nd Ed., MacMillan Publications, Ltd. NY (1991) and BIOCATALYSTS IN ORGANIC SYNTHESES, Tramper *et al.*, Eds., Elsevier Science Publishers, Amsterdam, The Netherlands (1985). A variety of exemplary uses that illustrate this and similar aspects of the present invention are discussed below.

1. Biosynthetic Enzymes

Open reading frames encoding proteins involved in mediating the catalytic reactions involved in intermediary and macromolecular metabolism, the biosynthesis of small molecules, cellular processes and other functions includes enzymes involved in the degradation of the intermediary products of metabolism, enzymes involved in central intermediary metabolism, enzymes involved in respiration, both aerobic and anaerobic, enzymes involved in fermentation, enzymes involved in ATP proton motor force conversion, enzymes involved in broad regulatory function, enzymes involved in amino acid synthesis, enzymes involved in nucleotide synthesis, enzymes involved in cofactor and vitamin synthesis, can be used for industrial biosynthesis.

The various metabolic pathways present in *Streptococcus pneumoniae* can be identified based on absolute nutritional requirements as well as by examining the various enzymes identified in Table 1-3 and SEQ ID NOS:1-391.

Of particular interest are polypeptides involved in the degradation of intermediary metabolites as well as non-macromolecular metabolism. Such enzymes include amylases, glucose oxidases, and catalase.

Proteolytic enzymes are another class of commercially important enzymes. Proteolytic enzymes find use in a number of industrial processes including the processing of flax and other vegetable fibers, in the extraction, clarification and depectinization of fruit juices, in the extraction of vegetables' oil and in the maceration of fruits and vegetables to give unicellular fruits. A detailed review of the proteolytic enzymes used in the food industry is provided in Rombouts *et al.*,

Symbiosis 21:79 (1986) and Voragen *et al.* in *Biocatalysts In Agricultural Biotechnology*, Whitaker *et al.*, Eds., *American Chemical Society Symposium Series 389*:93 (1989).

The metabolism of sugars is an important aspect of the primary metabolism of *Streptococcus pneumoniae*. Enzymes involved in the degradation of sugars, such as, particularly, glucose, galactose, fructose and xylose, can be used in industrial fermentation. Some of the important sugar transforming enzymes, from a commercial viewpoint, include sugar isomerases such as glucose isomerase. Other metabolic enzymes have found commercial use such as glucose oxidases which produces ketogulonic acid (KGA). KGA is an intermediate in the commercial production of ascorbic acid using the Reichstein's procedure, as described in Krueger *et al.*, *Biotechnology* 6(A), Rhine *et al.*, Eds., Verlag Press, Weinheim, Germany (1984).

Glucose oxidase (GOD) is commercially available and has been used in purified form as well as in an immobilized form for the deoxygenation of beer. See, for instance, Hartmeir *et al.*, *Biotechnology Letters 1*:21 (1979). The most important application of GOD is the industrial scale fermentation of gluconic acid. Market for gluconic acids which are used in the detergent, textile, leather, photographic, pharmaceutical, food, feed and concrete industry, as described, for example, in Bigelis *et al.*, beginning on page 357 in GENE MANIPULATIONS AND FUNGI; Benett *et al.*, Eds., Academic Press, New York (1985). In addition to industrial applications, GOD has found applications in medicine for quantitative determination of glucose in body fluids recently in biotechnology for analyzing syrups from starch and cellulose hydrosylates. This application is described in Owusu *et al.*, *Biochem. et Biophysica. Acta. 872*:83 (1986), for instance.

The main sweetener used in the world today is sugar which comes from sugar beets and sugar cane. In the field of industrial enzymes, the glucose isomerase process shows the largest expansion in the market today. Initially, soluble enzymes were used and later immobilized enzymes were developed (Krueger *et al.*, *Biotechnology, The Textbook of Industrial Microbiology*, Sinauer Associated Incorporated, Sunderland, Massachusetts (1990)). Today, the use of glucose- produced high fructose syrups is by far the largest industrial business using immobilized enzymes. A review of the industrial use of these enzymes is provided by Jorgensen, Starch *40*:307 (1988).

Proteinases, such as alkaline serine proteinases, are used as detergent additives and thus represent one of the largest volumes of microbial enzymes used in the industrial sector. Because of their industrial importance, there is a large body of published and unpublished information regarding the use of these enzymes in industrial processes. (See Faultman *et al.*, Acid Proteases Structure Function and Biology, Tang, J., ed., Plenum Press, New York (1977) and Godfrey *et al.*, Industrial Enzymes, MacMillan Publishers, Surrey, UK (1983) and Hepner *et al.*, Report Industrial Enzymes by 1990, Hel Hepner & Associates, London (1986)).

Another class of commercially usable proteins of the present invention are the microbial lipases, described by, for instance, Macrae *et al.*, *Philosophical Transactions of the Chiral Society of London 310*:227 (1985) and Poserke, *Journal of the American Oil Chemist Society 61*:1758 (1984). A major use of lipases is in the fat and oil industry for the production of neutral glycerides using lipase catalyzed inter-esterification of readily available triglycerides. Application of lipases include the use as a detergent additive to facilitate the removal of fats from fabrics in the course of the washing procedures.

The use of enzymes, and in particular microbial enzymes, as catalyst for key steps in the synthesis of complex organic molecules is gaining popularity at a great rate. One area of great interest is the preparation of chiral intermediates. Preparation of chiral intermediates is of interest to a wide range of synthetic chemists particularly those scientists involved with the preparation of new pharmaceuticals, agrochemicals, fragrances and flavors. (See Davies *et al.*, *Recent Advances in the Generation of Chiral Intermediates Using Enzymes*, CRC Press, Boca Raton, Florida (1990)). The following reactions catalyzed by enzymes are of interest to organic chemists: hydrolysis of carboxylic acid esters, phosphate esters, amides and nitriles, esterification reactions, trans-esterification reactions, synthesis of amides, reduction of alkanones and oxoalkanates, oxidation of alcohols to carbonyl compounds, oxidation of sulfides to sulfoxides, and carbon bond forming reactions such as the aldol reaction.

When considering the use of an enzyme encoded by one of the ORFs of the present invention for biotransformation and organic synthesis it is sometimes necessary to consider the respective advantages and disadvantages of using a microorganism as opposed to an isolated enzyme. Pros and cons of using a whole cell system on the one hand or an isolated partially purified enzyme on the other

hand, has been described in detail by Bud *et al.*, Chemistry in Britain (1987), p. 127.

Amino transferases, enzymes involved in the biosynthesis and metabolism of amino acids, are useful in the catalytic production of amino acids. The advantages of using microbial based enzyme systems is that the amino transferase enzymes catalyze the stereo- selective synthesis of only L-amino acids and generally possess uniformly high catalytic rates. A description of the use of amino transferases for amino acid production is provided by Roselle-David, *Methods of Enzymology 136*:479 (1987).

Another category of useful proteins encoded by the ORFs of the present invention include enzymes involved in nucleic acid synthesis, repair, and recombination.

2. Generation of Antibodies

As described here, the proteins of the present invention, as well as homologs thereof, can be used in a variety of procedures and methods known in the art which are currently applied to other proteins. The proteins of the present invention can further be used to generate an antibody which selectively binds the protein. Such antibodies can be either monoclonal or polyclonal antibodies, as well fragments of these antibodies, and humanized forms.

The invention further provides antibodies which selectively bind to one of the proteins of the present invention and hybridomas which produce these antibodies. A hybridoma is an immortalized cell line which is capable of secreting a specific monoclonal antibody.

In general, techniques for preparing polyclonal and monoclonal antibodies as well as hybridomas capable of producing the desired antibody are well known in the art (Campbell, A. M., *Monoclonal Antibody Technology: Laboratory Techniques In Biochemistry And Molecular Biology*, Elsevier Science Publishers, Amsterdam, The Netherlands (1984); St. Groth *et al.*, *J. Immunol. Methods 35:* 1-21 (1980), Kohler and Milstein, *Nature 256*:495-497 (1975)), the trioma technique, the human B-cell hybridoma technique (Kozbor *et al.*, *Immunology Today 4*:72 (1983), pgs. 77-96 of Cole *et al.*, in *Monoclonal Antibodies And Cancer Therapy*, Alan R. Liss, Inc. (1985)). Any animal (mouse, rabbit, *etc.*) which is known to produce antibodies can be immunized with the pseudogene polypeptide. Methods for immunization are well known in the art. Such methods

include subcutaneous or interperitoneal injection of the polypeptide. One skilled in the art will recognize that the amount of the protein encoded by the ORF of the present invention used for immunization will vary based on the animal which is immunized, the antigenicity of the peptide and the site of injection.

The protein which is used as an immunogen may be modified or administered in an adjuvant in order to increase the protein's antigenicity. Methods of increasing the antigenicity of a protein are well known in the art and include, but are not limited to coupling the antigen with a heterologous protein (such as globulin or galactosidase) or through the inclusion of an adjuvant during immunization.

For monoclonal antibodies, spleen cells from the immunized animals are removed, fused with myeloma cells, such as SP2/0-Ag14 myeloma cells, and allowed to become monoclonal antibody producing hybridoma cells.

Any one of a number of methods well known in the art can be used to identify the hybridoma cell which produces an antibody with the desired characteristics. These include screening the hybridomas with an ELISA assay, western blot analysis, or radioimmunoassay (Lutz *et al.*, *Exp. Cell Res. 175:*109-124 (1988)).

Hybridomas secreting the desired antibodies are cloned and the class and subclass is determined using procedures known in the art (Campbell, A. M., *Monoclonal Antibody Technology: Laboratory Techniques in Biochemistry and Molecular Biology*, Elsevier Science Publishers, Amsterdam, The Netherlands (1984)).

Techniques described for the production of single chain antibodies (U. S. Patent 4,946,778) can be adapted to produce single chain antibodies to proteins of the present invention.

For polyclonal antibodies, antibody containing antisera is isolated from the immunized animal and is screened for the presence of antibodies with the desired specificity using one of the above-described procedures.

The present invention further provides the above- described antibodies in detectably labelled form. Antibodies can be detectably labelled through the use of radioisotopes, affinity labels (such as biotin, avidin, *etc.*), enzymatic labels (such as horseradish peroxidase, alkaline phosphatase, *etc.*) fluorescent labels (such as FITC or rhodamine, *etc.*), paramagnetic atoms, *etc.* Procedures for accomplishing such labeling are well-known in the art, for example see Sternberger *et al.*, *J. Histochem. Cytochem. 18:*315 (1970); Bayer, E. A. *et al.*, *Meth. Enzym. 62*:308

(1979); Engval, E. *et al.*, *Immunol. 109*:129 (1972); Goding, J. W., *J. Immunol. Meth. 13*:215 (1976)).

The labeled antibodies of the present invention can be used for *in vitro*, *in vivo*, and in situ assays to identify cells or tissues in which a fragment of the *Streptococcus pneumoniae* genome is expressed.

The present invention further provides the above-described antibodies immobilized on a solid support. Examples of such solid supports include plastics such as polycarbonate, complex carbohydrates such as agarose and sepharose, acrylic resins and such as polyacrylamide and latex beads. Techniques for coupling antibodies to such solid supports are well known in the art (Weir, D. M. *et al.*, "Handbook of Experimental Immunology" 4th Ed., Blackwell Scientific Publications, Oxford, England, Chapter 10 (1986); Jacoby, W. D. *et al.*, Meth. Enzym. 34 Academic Press, N. Y. (1974)). The immobilized antibodies of the present invention can be used for *in vitro*, *in vivo*, and in situ assays as well as for immunoaffinity purification of the proteins of the present invention.

3. Diagnostic Assays and Kits

The present invention further provides methods to identify the expression of one of the ORFs of the present invention, or homolog thereof, in a test sample, using one of the DFs or antibodies of the present invention.

In detail, such methods comprise incubating a test sample with one or more of the antibodies or one or more of the DFs of the present invention and assaying for binding of the DFs or antibodies to components within the test sample.

Conditions for incubating a DF or antibody with a test sample vary. Incubation conditions depend on the format employed in the assay, the detection methods employed, and the type and nature of the DF or antibody used in the assay. One skilled in the art will recognize that any one of the commonly available hybridization, amplification or immunological assay formats can readily be adapted to employ the DFs or antibodies of the present invention. Examples of such assays can be found in Chard, T., *An Introduction to Radioimmunoassay and Related Techniques*, Elsevier Science Publishers, Amsterdam, The Netherlands (1986); Bullock, G. R. *et al.*, *Techniques in Immunocytochemistry*, Academic Press, Orlando, FL Vol. 1 (1982), Vol. 2 (1983), Vol. 3 (1985); Tijssen, P., *Practice and Theory of Enzyme Immunoassays: Laboratory Techniques in Biochemistry and*

Molecular Biology, Elsevier Science Publishers, Amsterdam, The Netherlands (1985).

The test samples of the present invention include cells, protein or membrane extracts of cells, or biological fluids such as sputum, blood, serum, plasma, or urine. The test sample used in the above-described method will vary based on the assay format, nature of the detection method and the tissues, cells or extracts used as the sample to be assayed. Methods for preparing protein extracts or membrane extracts of cells are well known in the art and can be readily be adapted in order to obtain a sample which is compatible with the system utilized.

In another embodiment of the present invention, kits are provided which contain the necessary reagents to carry out the assays of the present invention.

Specifically, the invention provides a compartmentalized kit to receive, in close confinement, one or more containers which comprises: (a) a first container comprising one of the DFs or antibodies of the present invention; and (b) one or more other containers comprising one or more of the following: wash reagents, reagents capable of detecting presence of a bound DF or antibody.

In detail, a compartmentalized kit includes any kit in which reagents are contained in separate containers. Such containers include small glass containers, plastic containers or strips of plastic or paper. Such containers allows one to efficiently transfer reagents from one compartment to another compartment such that the samples and reagents are not cross-contaminated, and the agents or solutions of each container can be added in a quantitative fashion from one compartment to another. Such containers will include a container which will accept the test sample, a container which contains the antibodies used in the assay, containers which contain wash reagents (such as phosphate buffered saline, Tris-buffers, *etc.*), and containers which contain the reagents used to detect the bound antibody or DF.

Types of detection reagents include labelled nucleic acid probes, labelled secondary antibodies, or in the alternative, if the primary antibody is labelled, the enzymatic, or antibody binding reagents which are capable of reacting with the labelled antibody. One skilled in the art will readily recognize that the disclosed DFs and antibodies of the present invention can be readily incorporated into one of the established kit formats which are well known in the art.

4. Screening Assay for Binding Agents

Using the isolated proteins of the present invention, the present invention further provides methods of obtaining and identifying agents which bind to a protein encoded by one of the ORFs of the present invention or to one of the fragments and the *Streptococcus pneumoniae* fragment and contigs herein described.

In general, such methods comprise steps of:

(a) contacting an agent with an isolated protein encoded by one of the ORFs of the present invention, or an isolated fragment of the *Streptococcus pneumoniae* genome; and

(b) determining whether the agent binds to said protein or said fragment.

The agents screened in the above assay can be, but are not limited to, peptides, carbohydrates, vitamin derivatives, or other pharmaceutical agents. The agents can be selected and screened at random or rationally selected or designed using protein modeling techniques.

For random screening, agents such as peptides, carbohydrates, pharmaceutical agents and the like are selected at random and are assayed for their ability to bind to the protein encoded by the ORF of the present invention.

Alternatively, agents may be rationally selected or designed. As used herein, an agent is said to be "rationally selected or designed" when the agent is chosen based on the configuration of the particular protein. For example, one skilled in the art can readily adapt currently available procedures to generate peptides, pharmaceutical agents and the like capable of binding to a specific peptide sequence in order to generate rationally designed antipeptide peptides, for example see Hurby *et al.*, "Application of Synthetic Peptides: Antisense Peptides," in *Synthetic Peptides, A User's Guide*, W. H. Freeman, NY (1992), pp. 289-307, and Kaspczak *et al.*, *Biochemistry 28*:9230-8 (1989), or pharmaceutical agents, or the like.

In addition to the foregoing, one class of agents of the present invention, as broadly described, can be used to control gene expression through binding to one of the ORFs or EMFs of the present invention. As described above, such agents can be randomly screened or rationally designed/selected. Targeting the ORF or EMF allows a skilled artisan to design sequence specific or element specific agents, modulating the expression of either a single ORF or multiple ORFs which rely on the same EMF for expression control.

One class of DNA binding agents are agents which contain base residues which hybridize or form a triple helix by binding to DNA or RNA. Such agents can be based on the classic phosphodiester, ribonucleic acid backbone, or can be a variety of sulfhydryl or polymeric derivatives which have base attachment capacity.

Agents suitable for use in these methods usually contain 20 to 40 bases and are designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee *et al.*, *Nucl. Acids Res.* 6:3073 (1979); Cooney *et al.*, *Science 241*:456 (1988); and Dervan *et al.*, *Science 251*:1360 (1991)) or to the mRNA itself (antisense - Okano, *J. Neurochem.* 56:560 (1991); *Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression*, CRC Press, Boca Raton, FL (1988)). Triple helix- formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques have been demonstrated to be effective in model systems. Information contained in the sequences of the present invention can be used to design antisense and triple helix-forming oligonucleotides, and other DNA binding agents.

5. Pharmaceutical Compositions and Vaccines

The present invention further provides pharmaceutical agents which can be used to modulate the growth or pathogenicity of *Streptococcus pneumoniae*, or another related organism, *in vivo* or *in vitro*. As used herein, a "pharmaceutical agent" is defined as a composition of matter which can be formulated using known techniques to provide a pharmaceutical compositions. As used herein, the "pharmaceutical agents of the present invention" refers the pharmaceutical agents which are derived from the proteins encoded by the ORFs of the present invention or are agents which are identified using the herein described assays.

As used herein, a pharmaceutical agent is said to "modulate the growth pathogenicity of *Streptococcus pneumoniae* or a related organism, *in vivo* or *in vitro*," when the agent reduces the rate of growth, rate of division, or viability of the organism in question. The pharmaceutical agents of the present invention can modulate the growth or pathogenicity of an organism in many fashions, although an understanding of the underlying mechanism of action is not needed to practice the use of the pharmaceutical agents of the present invention. Some agents will modulate the growth by binding to an important protein thus blocking the biological activity of the protein, while other agents may bind to a component of the outer

surface of the organism blocking attachment or rendering the organism more prone to act the bodies nature immune system. Alternatively, the agent may comprise a protein encoded by one of the ORFs of the present invention and serve as a vaccine. The development and use of a vaccine based on outer membrane components are well known in the art.

As used herein, a "related organism" is a broad term which refers to any organism whose growth can be modulated by one of the pharmaceutical agents of the present invention. In general, such an organism will contain a homolog of the protein which is the target of the pharmaceutical agent or the protein used as a vaccine. As such, related organisms do not need to be bacterial but may be fungal or viral pathogens.

The pharmaceutical agents and compositions of the present invention may be administered in a convenient manner, such as by the oral, topical, intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal or intradermal routes. The pharmaceutical compositions are administered in an amount which is effective for treating and/or prophylaxis of the specific indication. In general, they are administered in an amount of at least about 1 mg/kg body weight and in most cases they will be administered in an amount not in excess of about 1 g/kg body weight per day. In most cases, the dosage is from about 0.1 mg/kg to about 10 g/kg body weight daily, taking into account the routes of administration, symptoms, *etc.*

The agents of the present invention can be used in native form or can be modified to form a chemical derivative. As used herein, a molecule is said to be a "chemical derivative" of another molecule when it contains additional chemical moieties not normally a part of the molecule. Such moieties may improve the molecule's solubility, absorption, biological half life, *etc.* The moieties may alternatively decrease the toxicity of the molecule, eliminate or attenuate any undesirable side effect of the molecule, *etc.* Moieties capable of mediating such effects are disclosed in, among other sources, REMINGTON'S PHARMACEUTICAL SCIENCES (1980) cited elsewhere herein.

For example, such moieties may change an immunological character of the functional derivative, such as affinity for a given antibody. Such changes in immunomodulation activity are measured by the appropriate assay, such as a competitive type immunoassay. Modifications of such protein properties as redox or thermal stability, biological half-life, hydrophobicity, susceptibility to proteolytic degradation or the tendency to aggregate with carriers or into multimers also may

be effected in this way and can be assayed by methods well known to the skilled artisan.

The therapeutic effects of the agents of the present invention may be obtained by providing the agent to a patient by any suitable means (*e.g.*, inhalation, intravenously, intramuscularly, subcutaneously, enterally, or parenterally). It is preferred to administer the agent of the present invention so as to achieve an effective concentration within the blood or tissue in which the growth of the organism is to be controlled. To achieve an effective blood concentration, the preferred method is to administer the agent by injection. The administration may be by continuous infusion, or by single or multiple injections.

In providing a patient with one of the agents of the present invention, the dosage of the administered agent will vary depending upon such factors as the patient's age, weight, height, sex, general medical condition, previous medical history, *etc.* In general, it is desirable to provide the recipient with a dosage of agent which is in the range of from about 1 pg/kg to 10 mg/kg (body weight of patient), although a lower or higher dosage may be administered. The therapeutically effective dose can be lowered by using combinations of the agents of the present invention or another agent.

As used herein, two or more compounds or agents are said to be administered "in combination" with each other when either (1) the physiological effects of each compound, or (2) the serum concentrations of each compound can be measured at the same time. The composition of the present invention can be administered concurrently with, prior to, or following the administration of the other agent.

The agents of the present invention are intended to be provided to recipient subjects in an amount sufficient to decrease the rate of growth (as defined above) of the target organism.

The administration of the agent(s) of the invention may be for either a "prophylactic" or "therapeutic" purpose. When provided prophylactically, the agent(s) are provided in advance of any symptoms indicative of the organisms growth. The prophylactic administration of the agent(s) serves to prevent, attenuate, or decrease the rate of onset of any subsequent infection. When provided therapeutically, the agent(s) are provided at (or shortly after) the onset of an indication of infection. The therapeutic administration of the compound(s)

serves to attenuate the pathological symptoms of the infection and to increase the rate of recovery.

The agents of the present invention are administered to a subject, such as a mammal, or a patient, in a pharmaceutically acceptable form and in a therapeutically effective concentration. A composition is said to be "pharmacologically acceptable" if its administration can be tolerated by a recipient patient. Such an agent is said to be administered in a "therapeutically effective amount" if the amount administered is physiologically significant. An agent is physiologically significant if its presence results in a detectable change in the physiology of a recipient patient.

The agents of the present invention can be formulated according to known methods to prepare pharmaceutically useful compositions, whereby these materials, or their functional derivatives, are combined in a mixture with a pharmaceutically acceptable carrier vehicle. Suitable vehicles and their formulation, inclusive of other human proteins, *e.g.*, human serum albumin, are described, for example, in REMINGTON'S PHARMACEUTICAL SCIENCES, 16th Ed., Osol, A., Ed., Mack Publishing, Easton PA (1980). In order to form a pharmaceutically acceptable composition suitable for effective administration, such compositions will contain an effective amount of one or more of the agents of the present invention, together with a suitable amount of carrier vehicle.

Additional pharmaceutical methods may be employed to control the duration of action. Control release preparations may be achieved through the use of polymers to complex or absorb one or more of the agents of the present invention. The controlled delivery may be effectuated by a variety of well known techniques, including formulation with macromolecules such as, for example, polyesters, polyamino acids, polyvinyl, pyrrolidone, ethylenevinylacetate, methylcellulose, carboxymethylcellulose, or protamine, sulfate, adjusting the concentration of the macromolecules and the agent in the formulation, and by appropriate use of methods of incorporation, which can be manipulated to effectuate a desired time course of release. Another possible method to control the duration of action by controlled release preparations is to incorporate agents of the present invention into particles of a polymeric material such as polyesters, polyamino acids, hydrogels, poly(lactic acid) or ethylene vinylacetate copolymers. Alternatively, instead of incorporating these agents into polymeric particles, it is possible to entrap these materials in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization with, for example, hydroxymethylcellulose or gelatine-

microcapsules and poly(methylmethacylate) microcapsules, respectively, or in colloidal drug delivery systems, for example, liposomes, albumin microspheres, microemulsions, nanoparticles, and nanocapsules or in macroemulsions. Such techniques are disclosed in REMINGTON'S PHARMACEUTICAL SCIENCES (1980).

The invention further provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

In addition, the agents of the present invention may be employed in conjunction with other therapeutic compounds.

6. Shot-Gun Approach to Megabase DNA Sequencing

The present invention further demonstrates that a large sequence can be sequenced using a random shotgun approach. This procedure, described in detail in the examples that follow, has eliminated the up front cost of isolating and ordering overlapping or contiguous subclones prior to the start of the sequencing protocols.

Certain aspects of the present invention are described in greater detail in the examples that follow. The examples are provided by way of illustration. Other aspects and embodiments of the present invention are contemplated by the inventors, as will be clear to those of skill in the art from reading the present disclosure.

ILLUSTRATIVE EXAMPLES

LIBRARIES AND SEQUENCING

1. Shotgun Sequencing Probability Analysis

The overall strategy for a shotgun approach to whole genome sequencing follows from the Lander and Waterman (Landerman and Waterman, *Genomics* 2:231 (1988)) application of the equation for the Poisson distribution. According to this treatment, the probability, P , that any given base in a sequence of size L, in nucleotides, is not sequenced after a certain amount, n, in nucleotides, of random

sequence has been determined can be calculated by the equation $P = e^{-m}$, where m is L/n, the fold coverage. For instance, for a genome of 2.8 Mb, m=1 when 2.8 Mb of sequence has been randomly generated (1X coverage). At that point, $P = e^{-1} = 0.37$. The probability that any given base has not been sequenced is the same as the probability that any region of the whole sequence L has not been determined and, therefore, is equivalent to the fraction of the whole sequence that has yet to be determined. Thus, at one-fold coverage, approximately 37% of a polynucleotide of size L, in nucleotides has not been sequenced. When 14 Mb of sequence has been generated, coverage is 5X for a 2.8 Mb and the unsequenced fraction drops to .0067 or 0.67%. 5X coverage of a 2.8 Mb sequence can be attained by sequencing approximately 17,000 random clones from both insert ends with an average sequence read length of 410 bp.

Similarly, the total gap length, G, is determined by the equation $G = Le^{-m}$, and the average gap size, g, follows the equation, g = L/n. Thus, 5X coverage leaves about 240 gaps averaging about 82 bp in size in a sequence of a polynucleotide 2.8 Mb long.

The treatment above is essentially that of Lander and Waterman, *Genomics* 2: 231 (1988).

2. Random Library Construction

In order to approximate the random model described above during actual sequencing, a nearly ideal library of cloned genomic fragments is required. The following library construction procedure was developed to achieve this end.

Streptococcus pneumoniae DNA is prepared by phenol extraction. A mixture containing 200 µg DNA in 1.0 ml of 300 mM sodium acetate, 10 mM Tris-HCl, 1 mM Na-EDTA, 50% glycerol is processed through a nebulizer (IPI Medical Products) with a stream of nitrogen adjusted to 35 Kpa for 2 minutes. The sonicated DNA is ethanol precipitated and redissolved in 500 µl TE buffer.

To create blunt-ends, a 100 µl aliquot of the resuspended DNA is digested with 5 units of BAL31 nuclease (New England BioLabs) for 10 min at 30°C in 200 µl BAL31 buffer. The digested DNA is phenol-extracted, ethanol-precipitated, redissolved in 100 µl TE buffer, and then size-fractionated by electrophoresis through a 1.0% low melting temperature agarose gel. The section containing DNA fragments 1.6-2.0 kb in size is excised from the gel, and the LGT agarose is melted and the resulting solution is extracted with phenol to separate the agarose from the

DNA. DNA is ethanol precipitated and redissolved in 20 µl of TE buffer for ligation to vector.

A two-step ligation procedure is used to produce a plasmid library with 97% inserts, of which >99% were single inserts. The first ligation mixture (50 ul) contains 2 µg of DNA fragments, 2 µg pUC18 DNA (Pharmacia) cut with SmaI and dephosphorylated with bacterial alkaline phosphatase, and 10 units of T4 ligase (GIBCO/BRL) and is incubated at 14°C for 4 hr. The ligation mixture then is phenol extracted and ethanol precipitated, and the precipitated DNA is dissolved in 20 µl TE buffer and electrophoresed on a 1.0% low melting agarose gel. Discrete bands in a ladder are visualized by ethidium bromide-staining and UV illumination and identified by size as insert (I), vector (v), v+I, v+2i, v+3i, *etc.* The portion of the gel containing v+I DNA is excised and the v+I DNA is recovered and resuspended into 20 µl TE. The v+I DNA then is blunt-ended by T4 polymerase treatment for 5 min. at 37°C in a reaction mixture (50 ul) containing the v+I linears, 500 µM each of the 4 dNTPs, and 9 units of T4 polymerase (New England BioLabs), under recommended buffer conditions. After phenol extraction and ethanol precipitation the repaired v+I linears are dissolved in 20 µl TE. The final ligation to produce circles is carried out in a 50 µl reaction containing 5 µl of v+I linears and 5 units of T4 ligase at 14°C overnight. After 10 min. at 70°C the following day, the reaction mixture is stored at -20°C.

This two-stage procedure results in a molecularly random collection of single-insert plasmid recombinants with minimal contamination from double-insert chimeras (<1%) or free vector (<3%).

Since deviation from randomness can arise from propagation the DNA in the host, *E. coli* host cells deficient in all recombination and restriction functions (A. Greener, *Strategies 3 (1)*:5 (1990)) are used to prevent rearrangements, deletions, and loss of clones by restriction. Furthermore, transformed cells are plated directly on antibiotic diffusion plates to avoid the usual broth recovery phase which allows multiplication and selection of the most rapidly growing cells.

Plating is carried out as follows. A 100 µl aliquot of Epicurian Coli SURE II Supercompetent Cells (Stratagene 200152) is thawed on ice and transferred to a chilled Falcon 2059 tube on ice. A 1.7 µl aliquot of 1.42 M beta-mercaptoethanol is added to the aliquot of cells to a final concentration of 25 mM. Cells are incubated on ice for 10 min. A 1 µl aliquot of the final ligation is added to the cells and incubated on ice for 30 min. The cells are heat pulsed for 30 sec. at 42°C and

placed back on ice for 2 min. The outgrowth period in liquid culture is eliminated from this protocol in order to minimize the preferential growth of any given transformed cell. Instead the transformation mixture is plated directly on a nutrient rich SOB plate containing a 5 ml bottom layer of SOB agar (5% SOB agar: 20 g tryptone, 5 g yeast extract, 0.5 g NaCl, 1.5% Difco Agar per liter of media). The 5 ml bottom layer is supplemented with 0.4 ml of 50 mg/ml ampicillin per 100 ml SOB agar. The 15 ml top layer of SOB agar is supplemented with 1 ml X-Gal (2%), 1 ml MgCl (1 M), and 1 ml MgSO /100 ml SOB agar. The 15 ml top layer is poured just prior to plating. Our titer is approximately 100 colonies/10 µl aliquot of transformation.[2] [4]

All colonies are picked for template preparation regardless of size. Thus, only clones lost due to "poison" DNA or deleterious gene products are deleted from the library, resulting in a slight increase in gap number over that expected.

3. Random DNA Sequencing

High quality double stranded DNA plasmid templates are prepared using a "boiling bead" method developed in collaboration with Advanced Genetic Technology Corp. (Gaithersburg, MD) (Adams *et al.*, *Science 252*:1651 (1991); Adams *et al.*, *Nature 355*:632 (1992)). Plasmid preparation is performed in a 96-well format for all stages of DNA preparation from bacterial growth through final DNA purification. Template concentration is determined using Hoechst Dye and a Millipore Cytofluor. DNA concentrations are not adjusted, but low-yielding templates are identified where possible and not sequenced.

Templates are also prepared from two *Streptococcus pneumoniae* lambda genomic libraries. An amplified library is constructed in the vector Lambda GEM-12 (Promega) and an unamplified library is constructed in Lambda DASH II (Stratagene). In particular, for the unamplified lambda library, *Streptococcus pneumoniae* DNA (> 100 kb) is partially digested in a reaction mixture (200 ul) containing 50 µg DNA, 1X Sau3AI buffer, 20 units Sau3AI for 6 min. at 23°C. The digested DNA was phenol-extracted and electrophoresed on a 0.5% low melting agarose gel at 2V/cm for 7 hours. Fragments from 15 to 25 kb are excised and recovered in a final volume of 6 ul. One µl of fragments is used with 1 µl of DASHII vector (Stratagene) in the recommended ligation reaction. One µl of the ligation mixture is used per packaging reaction following the recommended protocol with the Gigapack II XL Packaging Extract (Stratagene, #227711). Phage

are plated directly without amplification from the packaging mixture (after dilution with 500 µl of recommended SM buffer and chloroform treatment). Yield is about $2.5x10^3$ pfu/ul. The amplified library is prepared essentially as above except the lambda GEM-12 vector is used. After packaging, about $3.5x10^4$ pfu are plated on the restrictive NM539 host. The lysate is harvested in 2 ml of SM buffer and stored frozen in 7% dimethylsulfoxide. The phage titer is approximately $1x10^9$ pfu/ml.

Liquid lysates (100 µl) are prepared from randomly selected plaques (from the unamplified library) and template is prepared by long-range PCR using T7 and T3 vector-specific primers.

Sequencing reactions are carried out on plasmid and/or PCR templates using the AB Catalyst LabStation with Applied Biosystems PRISM Ready Reaction Dye Primer Cycle Sequencing Kits for the M13 forward (M13-21) and the M13 reverse (M13RP1) primers (Adams *et al.*, *Nature 368*:474 (1994)). Dye terminator sequencing reactions are carried out on the lambda templates on a Perkin-Elmer 9600 Thermocycler using the Applied Biosystems Ready Reaction Dye Terminator Cycle Sequencing kits. T7 and SP6 primers are used to sequence the ends of the inserts from the Lambda GEM-12 library and T7 and T3 primers are used to sequence the ends of the inserts from the Lambda DASH II library. Sequencing reactions are performed by eight individuals using an average of fourteen AB 373 DNA Sequencers per day. All sequencing reactions are analyzed using the Stretch modification of the AB 373, primarily using a 34 cm well-to-read distance. The overall sequencing success rate very approximately is about 85% for M13-21 and M13RP1 sequences and 65% for dye-terminator reactions. The average usable read length is 485 bp for M13-21 sequences, 445bp for M13RP1 sequences, and 375 bp for dye-terminator reactions.

Richards *et al.*, Chapter 28 in AUTOMATED DNA SEQUENCING AND ANALYSIS, M. D. Adams, C. Fields, J. C. Venter, Eds., Academic Press, London, (1994) described the value of using sequence from both ends of sequencing templates to facilitate ordering of contigs in shotgun assembly projects of lambda and cosmid clones. We balance the desirability of both-end sequencing (including the reduced cost of lower total number of templates) against shorter read-lengths for sequencing reactions performed with the M13RP1 (reverse) primer compared to the M13-21 (forward) primer. Approximately one-half of the templates are sequenced from both ends. Random reverse sequencing reactions are

done based on successful forward sequencing reactions. Some M13RP1 sequences are obtained in a semi-directed fashion: M13-21: sequences pointing outward at the ends of contigs are chosen for M13RP1 sequencing in an effort to specifically order contigs.

5

4. Protocol for Automated Cycle Sequencing

The sequencing is carried out using ABI Catalyst robots and AB 373 Automated DNA Sequencers. The Catalyst robot is a publicly available sophisticated pipetting and temperature control robot which has been developed 10 specifically for DNA sequencing reactions. The Catalyst combines pre-aliquoted templates and reaction mixes consisting of deoxy- and dideoxynucleotides, the thermostable Taq DNA polymerase, fluorescently-labelled sequencing primers, and reaction buffer. Reaction mixes and templates are combined in the wells of an aluminum 96-well thermocycling plate. Thirty consecutive cycles of linear 15 amplification (*i.e.*., one primer synthesis) steps are performed including denaturation, annealing of primer and template, and extension; *i.e.*, DNA synthesis. A heated lid with rubber gaskets on the thermocycling plate prevents evaporation without the need for an oil overlay.

Two sequencing protocols are used: one for dye-labelled primers and a 20 second for dye-labelled dideoxy chain terminators. The shotgun sequencing involves use of four dye-labelled sequencing primers, one for each of the four terminator nucleotide. Each dye-primer is labelled with a different fluorescent dye, permitting the four individual reactions to be combined into one lane of the 373 DNA Sequencer for electrophoresis, detection, and base-calling. ABI currently 25 supplies pre-mixed reaction mixes in bulk packages containing all the necessary non-template reagents for sequencing. Sequencing can be done with both plasmid and PCR- generated templates with both dye-primers and dye- terminators with approximately equal fidelity, although plasmid templates generally give longer usable sequences.

30 Thirty-two reactions are loaded per AB373 Sequencer each day, for a total of 960 samples. Electrophoresis is run overnight following the manufacturer's protocols, and the data is collected for twelve hours. Following electrophoresis and fluorescence detection, the ABI 373 performs automatic lane tracking and base-calling. The lane-tracking is confirmed visually. Each sequence electropherogram 35 (or fluorescence lane trace) is inspected visually and assessed for quality. Trailing

sequences of low quality are removed and the sequence itself is loaded via software to a Sybase database (archived daily to 8mm tape). Leading vector polylinker sequence is removed automatically by a software program. Average edited lengths of sequences from the standard ABI 373 are around 400 bp and depend mostly on the quality of the template used for the sequencing reaction. ABI 373 Sequencers converted to Stretch Liners provide a longer electrophoresis path prior to fluorescence detection and increase the average number of usable bases to 500-600 bp.

INFORMATICS

1. Data Management

A number of information management systems for a large-scale sequencing lab have been developed. (For review see, for instance, Kerlavage *et al.*, *Proceedings of the Twenty-Sixth Annual Hawaii International Conference on System Sciences*, IEEE Computer Society Press, Washington D. C., 585 (1993)) The system used to collect and assemble the sequence data was developed using the Sybase relational database management system and was designed to automate data flow wherever possible and to reduce user error. The database stores and correlates all information collected during the entire operation from template preparation to final analysis of the genome. Because the raw output of the ABI 373 Sequencers was based on a Macintosh platform and the data management system chosen was based on a Unix platform, it was necessary to design and implement a variety of multi- user, client-server applications which allow the raw data as well as analysis results to flow seamlessly into the database with a minimum of user effort.

2. Assembly

An assembly engine (TIGR Assembler) developed for the rapid and accurate assembly of thousands of sequence fragments was employed to generate contigs. The TIGR assembler simultaneously clusters and assembles fragments of the genome. In order to obtain the speed necessary to assemble more than 10^4 fragments, the algorithm builds a hash table of 12 bp oligonucleotide subsequences to generate a list of potential sequence fragment overlaps. The number of potential overlaps for each fragment determines which fragments are likely to fall into repetitive elements. Beginning with a single seed sequence fragment, TIGR Assembler extends the current contig by attempting to add the best matching

fragment based on oligonucleotide content. The contig and candidate fragment are aligned using a modified version of the Smith-Waterman algorithm which provides for optimal gapped alignments (Waterman, M. S., *Methods in Enzymology 164*:765 (1988)). The contig is extended by the fragment only if strict criteria for the quality of the match are met. The match criteria include the minimum length of overlap, the maximum length of an unmatched end, and the minimum percentage match. These criteria are automatically lowered by the algorithm in regions of minimal coverage and raised in regions with a possible repetitive element. The number of potential overlaps for each fragment determines which fragments are likely to fall into repetitive elements. Fragments representing the boundaries of repetitive elements and potentially chimeric fragments are often rejected based on partial mismatches at the ends of alignments and excluded from the current contig. TIGR Assembler is designed to take advantage of clone size information coupled with sequencing from both ends of each template. It enforces the constraint that sequence fragments from two ends of the same template point toward one another in the contig and are located within a certain range of base pairs (definable for each clone based on the known clone size range for a given library).

The process resulted in 391 contigs as represented by SEQ ID NOs:1-391.

3. Identifying Genes

The predicted coding regions of the *Streptococcus pneumoniae* genome were initially defined with the program GeneMark, which finds ORFs using a probabilistic classification technique. The predicted coding region sequences were used in searches against a database of all nucleotide sequences from GenBank (October, 1997), using the BLASTN search method to identify overlaps of 50 or more nucleotides with at least a 95% identity. Those ORFs with nucleotide sequence matches are shown in Table 1. The ORFs without such matches were translated to protein sequences and compared to a non-redundant database of known proteins generated by combining the Swiss-prot, PIR and GenPept databases. ORFs that matched a database protein with BLASTP probability less than or equal to 0.01 are shown in Table 2. The table also lists assigned functions based on the closest match in the databases. ORFs that did not match protein or nucleotide sequences in the databases at these levels are shown in Table 3.

ILLUSTRATIVE APPLICATIONS

1. Production of an Antibody to a *Streptococcus pneumoniae* Protein

Substantially pure protein or polypeptide is isolated from the transfected or transformed cells using any one of the methods known in the art. The protein can also be produced in a recombinant prokaryotic expression system, such as *E. coli*, or can be chemically synthesized. Concentration of protein in the final preparation is adjusted, for example, by concentration on an Amicon filter device, to the level of a few micrograms/ml. Monoclonal or polyclonal antibody to the protein can then be prepared as follows.

2. Monoclonal Antibody Production by Hybridoma Fusion

Monoclonal antibody to epitopes of any of the peptides identified and isolated as described can be prepared from murine hybridomas according to the classical method of Kohler, G. and Milstein, C., *Nature 256*:495 (1975) or modifications of the methods thereof. Briefly, a mouse is repetitively inoculated with a few micrograms of the selected protein over a period of a few weeks. The mouse is then sacrificed, and the antibody producing cells of the spleen isolated. The spleen cells are fused by means of polyethylene glycol with mouse myeloma cells, and the excess unfused cells destroyed by growth of the system on selective media comprising aminopterin (HAT media). The successfully fused cells are diluted and aliquots of the dilution placed in wells of a microtiter plate where growth of the culture is continued. Antibody-producing clones are identified by detection of antibody in the supernatant fluid of the wells by immunoassay procedures, such as ELISA, as originally described by Engvall, E., *Meth. Enzymol. 70:*419 (1980), and modified methods thereof. Selected positive clones can be expanded and their monoclonal antibody product harvested for use. Detailed procedures for monoclonal antibody production are described in Davis, L. *et al.*, *Basic Methods in Molecular Biology*, Elsevier, New York. Section 21-2 (1989).

3. Polyclonal Antibody Production by Immunization

Polyclonal antiserum containing antibodies to heterogenous epitopes of a single protein can be prepared by immunizing suitable animals with the expressed protein described above, which can be unmodified or modified to enhance immunogenicity. Effective polyclonal antibody production is affected by many factors related both to the antigen and the host species. For example, small molecules tend to be less immunogenic than others and may require the use of carriers and adjuvant. Also, host animals vary in response to site of inoculations and dose, with both inadequate or excessive doses of antigen resulting in low titer antisera. Small doses (ng level) of antigen administered at multiple intradermal sites appears to be most reliable. An effective immunization protocol for rabbits can be found in Vaitukaitis, J. *et al.*, *J. Clin.* Endocrinol. Metab. 33:988-991 (1971).

Booster injections can be given at regular intervals, and antiserum harvested when antibody titer thereof, as determined semi-quantitatively, for example, by double immunodiffusion in agar against known concentrations of the antigen, begins to fall. See, for example, Ouchterlony, O. *et al.*, Chap. 19 in: *Handbook of Experimental Immunology*, Wier, D., ed. Blackwell (1973). Plateau concentration of antibody is usually in the range of 0.1 to 0.2 mg/ml of serum (about 12M). Affinity of the antisera for the antigen is determined by preparing competitive binding curves, as described, for example, by Fisher, D., Chap. 42 in: *Manual of Clinical Immunology*, second edition, Rose and Friedman, eds., Amer. Soc. For Microbiology, Washington, D. C. (1980)

Antibody preparations prepared according to either protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi- quantitatively or qualitatively to identify the presence of antigen in a biological sample. In addition, antibodies are useful in various animal models of pneumococcal disease as a means of evaluating the protein used to make the antibody as a potential vaccine target or as a means of evaluating the antibody as a potential immunotherapeutic or immunoprophylactic reagent.

4. Preparation of PCR Primers and Amplification of DNA

Various fragments of the *Streptococcus pneumoniae* genome, such as those of Tables 1-3 and SEQ ID NOS:1-391 can be used, in accordance with the present invention, to prepare PCR primers for a variety of uses. The PCR primers are preferably at least 15 bases, and more preferably at least 18 bases in length. When selecting a primer sequence, it is preferred that the primer pairs have approximately the same G/C ratio, so that melting temperatures are approximately the same. The PCR primers and amplified DNA of this Example find use in the Examples that follow.

5. Gene expression from DNA Sequences Corresponding to ORFs

A fragment of the *Streptococcus pneumoniae* genome provided in Tables 1-3 is introduced into an expression vector using conventional technology. Techniques to transfer cloned sequences into expression vectors that direct protein translation in mammalian, yeast, insect or bacterial expression systems are well known in the art. Commercially available vectors and expression systems are available from a variety of suppliers including Stratagene (La Jolla, California), Promega (Madison, Wisconsin), and Invitrogen (San Diego, California). If desired, to enhance expression and facilitate proper protein folding, the codon context and codon pairing of the sequence may be optimized for the particular expression organism, as explained by Hatfield *et al.*, U. S. Patent No. 5,082,767, incorporated herein by this reference.

The following is provided as one exemplary method to generate polypeptide(s) from cloned ORFs of the *Streptococcus pneumoniae* genome fragment. Bacterial ORFs generally lack a poly A addition signal. The addition signal sequence can be added to the construct by, for example, splicing out the poly A addition sequence from pSG5 (Stratagene) using BglI and SalI restriction endonuclease enzymes and incorporating it into the mammalian expression vector pXT1 (Stratagene) for use in eukaryotic expression systems. pXT1 contains the LTRs and a portion of the gag gene of Moloney Murine Leukemia Virus. The positions of the LTRs in the construct allow efficient stable transfection. The vector includes the Herpes Simplex thymidine kinase promoter and the selectable neomycin gene. The *Streptococcus pneumoniae* DNA is obtained by PCR from the bacterial vector using oligonucleotide primers complementary to the *Streptococcus pneumoniae* DNA and containing restriction endonuclease sequences for PstI incorporated into the 5' primer and BglII at the 5' end of the corresponding *Streptococcus pneumoniae* DNA 3' primer, taking care to ensure that the *Streptococcus pneumoniae* DNA is positioned such that its followed with the poly A addition sequence. The purified fragment obtained from the resulting PCR reaction is digested with PstI, blunt ended with an exonuclease, digested with BglII, purified and ligated to pXT1, now containing a poly A addition sequence and digested BglII.

The ligated product is transfected into mouse NIH 3T3 cells using Lipofectin (Life Technologies, Inc., Grand Island, New York) under conditions outlined in the product specification. Positive transfectants are selected after growing the transfected cells in 600 ug/ml G418 (Sigma, St. Louis, Missouri). The protein is preferably released into the supernatant. However if the protein has membrane binding domains, the protein may additionally be retained within the cell or expression may be restricted to the cell surface. Since it may be necessary to purify and locate the transfected product, synthetic 15-mer peptides synthesized from the predicted *Streptococcus pneumoniae* DNA sequence are injected into mice to generate antibody to the polypeptide encoded by the *Streptococcus pneumoniae* DNA.

Alternatively and if antibody production ~~is not~~ possible, the *Streptococcus pneumoniae* DNA sequence is additionally incorporated into eukaryotic expression vectors and expressed as, for example, a globin fusion. Antibody to the globin moiety then is used to purify the chimeric protein. Corresponding protease cleavage sites are engineered between the globin moiety and the polypeptide encoded by the *Streptococcus pneumoniae* DNA so that the latter may be freed from the formed by simple protease digestion. One useful expression vector for generating globin chimerics is pSG5 (Stratagene). This vector encodes a rabbit globin. Intron II of the rabbit globin gene facilitates splicing of the expressed transcript, and the polyadenylation signal incorporated into the construct increases the level of expression. These techniques are well known to those skilled in the art of molecular biology. Standard methods are published in methods texts such as Davis *et al.*, cited elsewhere herein, and many of the methods are available from the technical assistance representatives from Stratagene, Life Technologies, Inc., or Promega. Polypeptides of the invention also may be produced using *in vitro* translation systems such as *in vitro* ExpressTM Translation Kit (Stratagene).

While the present invention has been described in some detail for purposes of clarity and understanding, one skilled in the art will appreciate that various changes in form and detail can be made without departing from the true scope of the invention.

All patents, patent applications and publications referred to above are hereby incorporated by reference.

TABLE 1

S. pneumoniae - Coding regions containing known sequences

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	percent ident	HSP nt length	ORF nt length
1	1	437	1003	gb|U41735|	Streptococcus pneumoniae peptide methionine sulfoxide reductase (msrA) and homoserine kinase homolog (thrB) genes, complete cds	92	200	567
2	5	6169	5720	gb|U04047|	Streptococcus pneumoniae SSZ dextran glucosidase gene and insertion sequence IS1202 transposase gene, complete cds	96	450	450
2	6	6592	6167	emb|Z83335|SPZ8	S.pneumoniae dexB, capI[A,B,C,D,E,F,G,H,I,J,K] genes, dTDP-rhamnose biosynthesis genes and aliA gene	98	426	426
3	11	9770	9147	emb|Z83335|SPZ8	S.pneumoniae dexB, capI[A,B,C,D,E,F,G,H,I,J,K] genes, dTDP-rhamnose biosynthesis genes and aliA gene	94	624	624
3	12	10489	9671	emb|Z83335|SPZ8	S.pneumoniae dexB, capI[A,B,C,D,E,F,G,H,I,J,K] genes, dTDP-rhamnose biosynthesis genes and aliA gene	91	819	819
3	13	11546	12019	gb|U43526|	Streptococcus pneumoniae neuraminidase B (nanB) gene, complete cds, and neuraminidase (nanA) gene, partial cds	99	474	474
3	14	12017	13375	gb|U43526|	Streptococcus pneumoniae neuraminidase B (nanB) gene, complete cds, and neuraminidase (nanA) gene, partial cds	99	1359	1359
3	15	13421	14338	gb|U43526|	Streptococcus pneumoniae neuraminidase B (nanB) gene, complete cds, and neuraminidase (nanA) gene, partial cds	99	918	918
3	16	14329	15171	gb|U43526|	Streptococcus pneumoniae neuraminidase B (nanB) gene, complete cds, and neuraminidase (nanA) gene, partial cds	99	843	843
3	17	15132	17282	gb|U43526|	Streptococcus pneumoniae neuraminidase B (nanB) gene, complete cds, and neuraminidase (nanA) gene, partial cds	99	2151	2151
3	18	17267	18397	gb|U43526|	Streptococcus pneumoniae neuraminidase B (nanB) gene, complete cds, and neuraminidase (nanA) gene, partial cds	99	1069	1131
4	1	46	1188	emb|Y11463|SPDN	Streptococcus pneumoniae dnaG, rpoD, cpoA genes and ORF3 and ORF5	99	1143	1143
4	2	1198	2529	emb|Y11463|SPDN	Streptococcus pneumoniae dnaG, rpoD, cpoA genes and ORF3 and ORF5	99	876	1332
5	7	11297	11473	gb|U41735|	Streptococcus pneumoniae peptide methionine sulfoxide reductase (msrA) and homoserine kinase homolog (thrB) genes, complete cds	82	175	177
6	7	7125	7364	emb|Z77726|SPIS	S.pneumoniae DNA for insertion sequence IS1318 (1372 bp)	93	238	240
6	8	7322	7570	emb|Z77725|SPIS	S.pneumoniae DNA for insertion sequence IS1381 (966 bp)	95	160	249
6	9	7533	7985	emb|Z77725|SPIS	S.pneumoniae DNA for insertion sequence IS1381 (966 bp)	99	453	453
6	23	20197	19733	emb|Z83335|SPZ8	S.pneumoniae dexB, capI[A,B,C,D,E,F,G,H,I,J,K] genes, dTDP-rhamnose biosynthesis genes and aliA gene	96	465	465
7	10	8305	7682	emb|Z83335|SPZ8	S.pneumoniae dexB, capI[A,B,C,D,E,F,G,H,I,J,K] genes, dTDP-rhamnose biosynthesis genes and aliA gene	95	624	624

TABLE 1

S. pneumoniae - Coding regions containing known sequences

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	percent ident	HSP nt length	ORF nt length
7	11	9024	8206	emb|Z83335|SPZ8	S.pneumoniae dexB, capI(A,B,C,D,E,F,G,H,I,J,K) genes, dTDP-rhamnose biosynthesis genes and aliA gene	95	819	819
10	11	9304	8078	gb|L29323|	Streptococcus pneumoniae methyl transferase (mtr) gene cluster, complete cds	93	513	1227
11	2	548	919	emb|Z79691|SOOR	S.pneumoniae yorf(A,B,C,D,E), ftsL, pbpX and regR genes	99	316	372
11	3	892	1980	emb|Z79691|SOOR	S.pneumoniae yorf(A,B,C,D,E), ftsL, pbpX and regR genes	99	1089	1089
11	5	3040	3477	emb|Z79691|SOOR	S.pneumoniae yorf(A,B,C,D,E), ftsL, pbpX and regR genes	99	259	438
11	6	3480	3247	emb|Z79691|SOOR	S.pneumoniae yorf(A,B,C,D,E), ftsL, pbpX and regR genes	99	234	234
11	7	3601	4557	emb|Z79691|SOOR	S.pneumoniae yorf(A,B,C,D,E), ftsL, pbpX and regR genes	98	957	957
11	8	4506	4886	emb|Z79691|SOOR	S.pneumoniae yorf(A,B,C,D,E), ftsL, pbpX and regR genes	99	381	381
11	9	4884	7142	emb|X16367|SPPB	Streptococcus pneumoniae pbpX gene for penicillin binding protein 2X	99	2259	2259
11	10	7132	8124	emb|X16367|SPPB	Streptococcus pneumoniae pbpX gene for penicillin binding protein 2X	98	70	993
13	1	53	1126	gb|M31296|	S.pneumoniae recP gene, complete cds	99	437	1074
14	3	1837	2148	emb|Z83335|SPZ8	S.pneumoniae dexB, capI(A,B,C,D,E,F,G,H,I,J,K) genes, dTDP-rhamnose biosynthesis genes and aliA gene	87	96	312
14	4	2518	2108	gb|M36180|	Streptococcus pneumoniae transposase, (comA and comB) and SAICAR synthetase (purC) genes, complete cds	98	411	411
15	9	8942	8511	gb|U09239|	Streptococcus pneumoniae type 19F capsular polysaccharide biosynthesis operon, (cps19FABCDEFGHIJKLMNO) genes, complete cds, and aliA gene, partial cds	89	340	432
17	7	3910	3458	emb|Z77726|SPIS	S.pneumoniae DNA for insertion sequence ISI318 (1372 bp)	98	453	453
17	8	4304	3873	emb|Z77727|SPIS	S.pneumoniae DNA for insertion sequence ISI318 (823 bp)	96	382	432
19	1	41	529	emb|X94909|SPIG	S.pneumoniae iga gene	75	368	489
19	2	554	757	gb|L07752|	Streptococcus pneumoniae attachment site (attB), DNA sequence	99	167	204
19	3	946	1827	gb|L07752|	Streptococcus pneumoniae attachment site (attB), DNA sequence	94	100	882
20	1	937	182	gb|U33315|	Streptococcus pneumoniae orfL gene, partial cds, competence stimulating peptide precursor (comC), histidine protein kinase (comD) and response regulator (comE) genes, complete cds, tRNA-Arg and tRNA-Gln genes	99	756	756
20	2	2271	931	gb|U33315|	Streptococcus pneumoniae orfL gene, partial cds, competence stimulating peptide precursor (comC), histidine protein kinase (comD) and response regulator (comE) genes, complete cds, tRNA-Arg and tRNA-Gln genes	98	1341	1341

TABLE 1

S. pneumoniae - Coding regions containing known sequences

Contig ID	ORF ID	Start (nt)	Stop (nt)	match accession	match gene name	percent ident	HSP nt length	ORF nt length
20	3	3175	2684	gb|U76218|	Streptococcus pneumoniae competence stimulating peptide precursor ComC (comC), histidine kinase homolog ComD (comD), and response regulator homolog ComE (comE) genes, complete cds	99	492	492
20	4	3322	4527	gb|AF000658|	Streptococcus pneumoniae R801 tRNA-Arg gene, partial sequence, and putative serine protease (sphtrA), SPSpoJ (spspoJ), initiator protein (spdnaA) and beta subunit of DNA polymerase III (spdnaN) genes, complete cds	99	1206	1206
20	5	4573	5343	gb|AF000658|	Streptococcus pneumoniae R801 tRNA-Arg gene, partial sequence, and putative serine protease (sphtrA), SPSpoJ (spspoJ), initiator protein (spdnaA) and beta subunit of DNA polymerase III (spdnaN) genes, complete cds	99	771	771
20	6	5532	6917	gb|AF000658|	Streptococcus pneumoniae R801 tRNA-Arg gene, partial sequence, and putative serine protease (sphtrA), SPSpoJ (spspoJ), initiator protein (spdnaA) and beta subunit of DNA polymerase III (spdnaN) genes, complete cds	99	1386	1386
20	7	6995	8212	gb|AF000658|	Streptococcus pneumoniae R801 tRNA-Arg gene, partial sequence, and putative serine protease (sphtrA), SPSpoJ (spspoJ), initiator protein (spdnaA) and beta subunit of DNA polymerase III (spdnaN) genes, complete cds	99	1218	1218
20	8	8214	8471	gb|AF000658|	Streptococcus pneumoniae R801 tRNA-Arg gene, partial sequence, and putative serine protease (sphtrA), SPSpoJ (spspoJ), initiator protein (spdnaA) and beta subunit of DNA polymerase III (spdnaN) genes, complete cds	98	258	258
20	9	8534	9670	gb|AF000658|	Streptococcus pneumoniae R801 tRNA-Arg gene, partial sequence, and putative serine protease (sphtrA), SPSpoJ (spspoJ), initiator protein (spdnaA) and beta subunit of DNA polymerase III (spdnaN) genes, complete cds	99	1134	1137
22	14	11887	12267	emb|Z77726|SP15	S.pneumoniae DNA for insertion sequence IS1318 (1372 bp)	99	226	381
22	15	12708	12256	emb|Z77727|SP15	S.pneumoniae DNA for insertion sequence IS1318 (823 bp)	97	353	453
22	16	13165	12662	emb|Z77726|SP15	S.pneumoniae DNA for insertion sequence IS1318 (1372 bp)	98	504	504
22	23	18398	18910	emb|Z66112|SP28	S.pneumoniae genes encoding galacturonosyl transferase and transposase and insertion sequence IS1515	95	463	513
22	24	18829	19299	emb|Z66112|SP28	S.pneumoniae genes encoding galacturonosyl transferase and transposase and insertion sequence IS1515	99	443	471
23	5	5624	4203	emb|X52474|SPPL	S.pneumoniae ply gene for pneumolysin	99	1422	1422
23	6	6063	5629	gb|M17717|	S.pneumoniae pneumolysin gene, complete cds	98	197	435
26	1	1500	2	emb|X94909|SPIG	S.pneumoniae iga gene	87	3487	5499
26	2	5823	5584	gb|U47687|	Streptococcus pneumoniae immunoglobulin A1 protease (iga) gene, complete cds	99	151	240
26	3	6878	5685	gb|U47681|	Streptococcus pneumoniae immunoglobulin A1 protease (iga) gene, complete cds	100	50	1194

TABLE 1

S. pneumoniae - Coding regions containing known sequences

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	percent ident	HSP nt length	ORF nt length
26	8	14498	14858	emb|Z83335|SPZ8	S.pneumoniae dexB, capI[A,B,C,D,E,F,G,H,I,J,K] genes, dTDP-rhamnose biosynthesis genes and aliA gene	99	338	357
26	9	14763	14924	emb|Z83335|SPZ8	S.pneumoniae dexB, capI[A,B,C,D,E,F,G,H,I,J,K] genes, dTDP-rhamnose biosynthesis genes and aliA gene	100	94	162
26	10	14922	15173	gb|U04047|	Streptococcus pneumoniae SSZ dextran glucosidase gene and insertion sequence IS1202 transposase gene, complete cds	97	242	252
28	1	80	505	emb|Z83335|SPZ8	S.pneumoniae dexB, capI[A,B,C,D,E,F,G,H,I,J,K] genes, dTDP-rhamnose biosynthesis genes and aliA gene	99	426	426
28	2	503	952	gb|U04047|	Streptococcus pneumoniae SSZ dextran glucosidase gene and insertion sequence IS1202 transposase gene, complete cds	97	450	450
28	3	780	1298	gb|U04047|	Streptococcus pneumoniae SSZ dextran glucosidase gene and insertion sequence IS1202 transposase gene, complete cds	96	181	519
34	1	207	1523	gb|L08611|	Streptococcus pneumoniae maltose/maltodextrin uptake (malX) and two maltodextrin permease (malC and malD) genes, complete cds	99	1317	1317
34	2	1477	2367	gb|L08611|	Streptococcus pneumoniae maltose/maltodextrin uptake (malX) and two maltodextrin permease (malC and malD) genes, complete cds	96	795	891
34	3	2593	3420	gb|L21856|	Streptococcus pneumoniae malA gene, complete cds; malR gene, complete cds	96	446	828
34	4	2790	2647	gb|L21856|	Streptococcus pneumoniae malA gene, complete cds; malR gene, complete cds	98	137	144
34	5	3418	4416	gb|L21856|	Streptococcus pneumoniae malA gene, complete cds; malR gene, complete cds	96	999	999
34	9	7764	7507	gb|U41735|	Streptococcus pneumoniae peptide methionine sulfoxide reductase (msrA) and homoserine kinase homolog (thrB) genes, complete cds	93	201	258
34	16	10562	10257	emb|X63602|SPBO	S.pneumoniae mmsA-Box	92	238	306
35	4	1176	1439	emb|Z83335|SPZ8	S.pneumoniae dexB, capI[A,B,C,D,E,F,G,H,I,J,K] genes, dTDP-rhamnose biosynthesis genes and aliA gene	87	248	264
35	5	1458	1961	gb|U09239|	Streptococcus pneumoniae type 19F capsular polysaccharide biosynthesis operon, (cps19fABCDEFGHIJKLMNO) genes, complete cds, and aliA gene, partial cds	98	264	504
35	17	16172	15477	emb|X85787|SPCP	S.pneumoniae dexB, cps14A, cps14B, cps14C, cps14D, cps14E, cps14F, cps14G, cps14H, cps14I, cps14J, cps14K, cps14L, tasA genes	97	696	696
35	18	16961	16170	emb|Z83335|SPZ8	S.pneumoniae dexB, capI[A,B,C,D,E,F,G,H,I,J,K] genes, dTDP-rhamnose biosynthesis genes and aliA gene	86	792	792
35	19	17620	16871	gb|U09239|	Streptococcus pneumoniae type 19F capsular polysaccharide biosynthesis operon, (cps19fABCDEFGHIJKLMNO) genes, complete cds, and aliA gene, partial cds	83	750	750

TABLE 1

S. pneumoniae - Coding regions containing known sequences

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	percent ident	HSP nt length	ORF nt length
35	20	19061	17604	emb|X85787|SPCP	S.pneumoniae dexB, cps14A, cps14B, cps14C, cps14D, cps14E, cps14F, cps14G, cps14H, cps14I, cps14J, cps14K, cps14L, tasA genes	94	1458	1458
36	19	18960	18352	gb|U40786|	Streptococcus pneumoniae surface antigen A variant precursor (psaA) and 18 kDa protein genes, complete cds, and ORF1 gene, partial cds	99	609	609
36	20	19934	18966	gb|U53509|	Streptococcus pneumoniae surface adhesin A precursor (psaA) gene, complete cds	99	969	969
37	1	2743	179	emb|Z67739|SPPA	S.pneumoniae parC, parE and transposase genes and unknown orf	99	2565	2565
37	2	2985	2824	emb|Z67739|SPPA	S.pneumoniae parC, parE and transposase genes and unknown orf	100	162	162
37	3	5034	3070	emb|Z67739|SPPA	S.pneumoniae parC, parE and transposase genes and unknown orf	99	1965	1965
37	4	5134	5790	emb|Z67739|SPPA	S.pneumoniae parC, parE and transposase genes and unknown orf	99	657	657
37	5	6171	5833	emb|Z67739|SPPA	S.pneumoniae parC, parE and transposase genes and unknown orf	96	339	339
38	19	12969	11268	gb|M28679|	S.pneumoniae promoter region DNA	100	64	300
39	2	1256	2137	gb|U41735|	Streptococcus pneumoniae peptide methionine sulfoxide reductase (msrA) and homoserine kinase homolog (thrB) genes, complete cds	99	882	882
39	3	2405	3370	gb|U41735|	Streptococcus pneumoniae peptide methionine sulfoxide reductase (msrA) and homoserine kinase homolog (thrB) genes, complete cds	99	966	966
40	9	5253	7208	gb|M29686|	S.pneumoniae mismatch repair (hexB) gene, complete cds	99	1956	1956
41	1	3	1037	emb|Z17307|SPRE	S.pneumoniae recA gene encoding RecA	99	1027	1035
41	2	1328	2713	emb|Z34303|SPCI	Streptococcus pneumoniae cin operon encoding the cinA, recA, dinF, lytA genes, and downstream sequences	99	1386	1386
41	3	3083	4045	gb|M13812|	S.pneumoniae autolysin (lytA) gene, complete cds	99	963	963
41	4	3272	3096	gb|M13812|	S.pneumoniae autolysin (lytA) gene, complete cds	100	177	177
41	5	3603	3860	gb|M13812|	S.pneumoniae autolysin (lytA) gene, complete cds	100	258	258
41	6	4755	5162	gb|L36660|	Streptocpccus pneumoniae ORF, complete cds	98	408	408
41	7	5270	5716	gb|L36660|	Streptocpccus pneumoniae ORF, complete cds	98	447	447
41	8	6112	6918	gb|L36660|	Streptococcus pneumoniae ORF, complete cds	98	431	807
41	9	6916	7119	gb|L36660|	Streptococcus pneumoniae ORF, complete cds	100	204	204
41	10	7082	7660	gb|L36660|	Streptococcus pneumoniae ORF, complete cds	97	552	579
41	11	7680	7979	gb|L36660|	Streptococcus pneumoniae ORF, complete cds	98	81	300
41	12	9169	8717	emb|Z77727|SPIS	S.pneumoniae DNA for insertion sequence IS1318 (823 bp)	97	353	453

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
228	2	1760	1942	|pir|F60663|F606	|translation elongation factor Tu - Streptococcus oralis	100	100	183
319	1	2	205	|gi|984927	|neomycin phosphotransferase (Cloning vector pBSL99)	100	100	204
260	1	2	1138	|pir|F60663|F606	|translation elongation factor Tu - Streptococcus oralis	99	98	1137
25	2	486	1394	|gi|1574495	|hypothetical (Haemophilus influenzae)	98	96	909
94	2	685	1002	|gi|310627	|phosphoenolpyruvate:sugar phosphotransferase system HPr (Streptococcus mutans)	98	93	318
312	1	190	2	|gi|347999	|ATP-dependent protease proteolytic subunit (Streptococcus salivarius)	98	95	189
329	1	1	807	|gi|924848	|inosine monophosphate dehydrogenase (Streptococcus pyogenes)	98	94	807
336	2	290	589	|gi|987050	|lacZ gene product (unidentified cloning vector)	98	98	300
181	9	5948	7366	|gi|153755	|phospho-beta-D-galactosidase (EC 3.2.1.85) (Lactococcus lactis cremoris)	97	94	1419
312	2	1044	361	|gi|347998	|uracil phosphoribosyltransferase (Streptococcus salivarius)	97	88	684
32	8	6575	7486	|sp|P37214|ERA_S	|GTP-BINDING PROTEIN ERA HOMOLOG.	96	91	912
94	3	951	2741	|gi|153615	|phosphoenolpyruvate:sugar phosphotransferase system enzyme I (Streptococcus salivarius)	96	92	1791
127	1	1	168	|gi|581299	|initiation factor IF-1 (Lactococcus lactis)	96	89	168
128	14	10438	11154	|gi|1276873	|DeoD (Streptococcus thermophilus)	96	93	717
181	4	1362	1598	|gi|46606	|lacD polypeptide (AA 1-326) (Staphylococcus aureus)	96	80	237
218	1	1	834	|gi|1743856	|intrageneric coaggregation-relevant adhesin (Streptococcus gordonii)	96	93	834
319	2	115	441	|gi|208225	|heat-shock protein 82/neomcyn phosphotransferase fusion protein (hsp82-neo) (unidentified cloning vector)	96	96	327
54	12	8622	10967	|gnl|PID|d100972	|Pyruvate formate-lyase (Streptococcus mutans)	95	89	2346
181	2	606	1289	|gi|149396	|lacD (Lactococcus lactis)	95	89	684
46	3	3410	3045	|gi|1850606	|YlxM (Streptococcus mutans)	94	86	366
89	10	7972	7337	|gi|703442	|thymidine kinase (Streptococcus gordonii)	94	86	636
148	9	6431	7354	|gi|995767	|UDP-glucose pyrophosphorylase (Streptococcus pyogenes)	94	85	924
160	7	4430	5848	|gi|153573	|H+ ATPase (Enterococcus faecalis)	94	87	1419
2	3	4598	3513	|gi|153763	|plasmin receptor (Streptococcus pyogenes)	93	86	1086
12	8	7877	6204	|gi|1103865	|formyl-tetrahydrofolate synthetase (Streptococcus mutans)	93	84	1674

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
65	11	4734	5120	gi|40150	L14 protein (AA 1-122) (Bacillus subtilis)	93	87	387
68	1	53	1297	gi|47341	antitumor protein (Streptococcus pyogenes)	93	87	1245
80	1	3	299	gnl|PID|d101166	ribosomal protein S7 (Bacillus subtilis)	93	84	297
127	3	695	1093	gi|142462	ribosomal protein S11 (Bacillus subtilis)	93	86	399
160	5	1924	3462	gi|1773264	ATPase, alpha subunit (Streptococcus mutans)	93	85	1539
211	5	3757	3047	gi|535273	aminopeptidase C (Streptococcus thermophilus)	93	82	711
262	1	16	564	gi|149394	lacB (Lactococcus lactis)	93	90	549
366	1	197	3	gi|295259	tryptophan synthase beta subunit (Synechocystis sp.)	93	91	195
25	3	1392	1976	gi|1574496	hypothetical (Haemophilus influenzae)	92	80	585
36	21	20781	19927	gi|310632	hydrophobic membrane protein (Streptococcus gordonii)	92	86	855
181	3	1265	1534	gi|149396	lacD (Lactococcus lactis)	92	83	270
181	7	3662	4060	gi|149410	enzyme III (Lactococcus lactis)	92	83	399
32	4	5631	3937	gnl|PID|e294090	fibronectin-binding protein-like protein A (Streptococcus gordonii)	91	85	1695
46	2	3054	1462	gi|1850607	signal recognition particle Ffh (Streptococcus mutans)	91	84	1593
65	10	4442	4726	pir|S17865|S178	ribosomal protein S17 - Bacillus stearothermophilus	91	80	285
77	2	260	1900	gi|287871	groEL gene product (Lactococcus lactis)	91	82	1641
84	1	2	2056	gi|871784	Clp-like ATP-dependent protease binding subunit (Bos taurus)	91	79	2055
99	8	10750	9272	gi|153740	sucrose phosphorylase (Streptococcus mutans)	91	84	1479
99	9	11947	11072	gi|153739	membrane protein (Streptococcus mutans)	91	78	876
127	5	2065	2469	pir|S07223|R5BS	ribosomal protein L17 - Bacillus stearothermophilus	91	78	405
132	6	9539	9390	gi|143065	hubst (Bacillus stearothermophilus)	91	89	150
137	8	4765	6153	gnl|PID|d100347	Na+ -ATPase beta subunit (Enterococcus hirae)	91	79	1389
151	7	11119	9734	gi|1815634	glutamine synthetase type I (Streptococcus agalactiae)	91	82	1386
201	2	1798	278	gi|2208998	dextran glucosidase DexS (Streptococcus suis)	91	79	1521
222	2	673	1839	gi|153741	ATP-binding protein (Streptococcus mutans)	91	85	1167
293	5	4113	4400	gi|1196921	unknown protein (insertion sequence IS861)	91	71	288
32	7	6166	6570	pir|A36933|A369	diacylglycerol kinase homolog - Streptococcus mutans	90	77	405

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
33	2	841	527	gi|1196921	unknown protein [insertion sequence IS861]	90	70	315
48	27	20908	19757	gni|PID|e274705	lactate oxidase [Streptococcus iniae]	90	80	1152
55	21	19777	18515	gni|PID|e221213	ClpX protein [Bacillus subtilis]	90	75	1263
56	2	717	977	gi|1710133	flagellar filament cap [Borrelia burgdorferi]	90	50	261
65	1	1	606	gi|1165303	L3 [Bacillus subtilis]	90	75	606
114	1	2	988	gi|153562	aspartate beta-semialdehyde dehydrogenase (EC 1.2.1.11) [Streptococcus mutans]	90	80	987
120	1	1345	827	gi|407880	ORF1 [Streptococcus equisimilis]	90	75	519
159	12	7690	8298	gi|143012	GMP synthetase [Bacillus subtilis]	90	84	609
166	4	4076	3282	gi|1661179	high affinity branched chain amino acid transport protein [Streptococcus mutans]	90	78	795
183	1	28	1395	gi|308858	ATP:pyruvate 2-O-phosphotransferase [Lactococcus lactis]	90	76	1368
191	3	2891	1662	gi|149521	tryptophan synthase beta subunit [Lactococcus lactis]	90	78	1230
198	2	1551	436	gi|2323342	(AF014460) CcpA [Streptococcus mutans]	90	76	1116
305	1	37	783	gi|1573551	asparagine synthetase A (asnA) [Haemophilus influenzae]	90	80	747
8	3	2285	3343	gi|149434	putative [Lactococcus lactis]	89	78	1059
46	8	7577	7362	pir|A45434|A454	ribosomal protein L19 - Bacillus stearothermophilus	89	76	216
49	9	8363	10342	gi|153792	recP peptide [Streptococcus pneumoniae]	89	83	1980
51	14	18410	19447	gi|308857	ATP:D-fructose 6-phosphate 1-phosphotransferase [Lactocccccus lactis]	89	81	1038
57	11	9686	10669	gni|PID|d100932	H2O-forming NADH Oxidase [Streptococcus mutans]	89	77	984
65	5	2418	2786	gi|1165307	S19 [Bacillus subtilis]	89	81	369
65	8	3806	4225	sp|P14577|RL16_	50S RIBOSOMAL PROTEIN L16.	89	82	420
65	18	8219	8719	gi|143417	ribosomal protein S5 [Bacillus stearothermophilus]	89	76	501
73	9	6337	5315	gi|532204	prs [Listeria monocytogenes]	89	70	1023
76	3	3360	1465	gni|PID|e200671	lepA gene product [Bacillus subtilis]	89	76	1896
99	10	12818	11919	gi|153738	membrane protein [Streptococcus mutans]	89	73	900
120	2	3552	1300	gi|407881	stringent response-like protein [Streptococcus equisimilis]	89	79	2253
122	5	4512	2791	gni|PID|e280490	unknown [Streptococcus pneumoniae]	89	81	1722

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
176	1	669	4	|gi|47394	|5-oxoprolyl-peptidase |Streptococcus pyogenes|	89	78	666
177	6	3050	3934	|gi|912423	|putative |Lactococcus lactis|	89	71	885
181	8	4033	5751	|gi|149411	|enzyme III |Lactococcus lactis|	89	80	1719
211	4	3149	2793	|gi|535273	|aminopeptidase C |Streptococcus thermophilus|	89	83	357
361	1	431	838	|gi|1196922	|unknown protein |Insertion sequence IS861|	89	70	408
34	17	11839	10535	|sp|P30059|SYH_S	|HISTIDYL-TRNA SYNTHETASE (EC 6.1.1.21) (HISTIDINE--TRNA LIGASE) (HISRS).	88	78	1305
38	3	1646	2623	|gi|2058544	|putative ABC transporter subunit ComYA |Streptococcus gordonii|	88	78	978
54	1	3	227	|gnl|PID|d101320	|YqgU |Bacillus subtilis|	88	66	225
57	2	611	1468	|gnl|PID|e13494	|putative reductase 1 |Saccharomyces cerevisiae|	88	75	858
65	13	5497	6069	|pir|A29102|R5BS	|ribosomal protein L5 - Bacillus stearothermophilus	88	75	573
65	20	9010	9500	|gi|2078381	|ribosomal protein L15 |Staphylococcus aureus|	88	83	471
78	3	3636	1108	|gnl|PID|d100781	|lysyl-aminopeptidase |Lactococcus lactis|	88	80	2529
106	12	12965	12054	|gi|2407215	|(AF017421) putative heat shock protein HtpX |Streptococcus gordonii|	88	72	912
107	2	219	962	|gnl|PID|e339862	|putative acylneuraminate lyase |Clostridium tertium|	88	75	744
111	8	14073	10420	|gi|402363	|RNA polymerase beta-subunit |Bacillus subtilis|	88	74	3654
126	9	13096	12062	|gnl|PID|e311468	|unknown |Bacillus subtilis|	88	74	1035
140	17	19143	18874	|gi|1573659	|H. influenzae predicted coding region HI0659 |Haemophilus influenzae|	88	61	270
144	1	394	555	|gnl|PID|e274705	|lactate oxidase |Streptococcus iniae|	88	75	162
148	4	2723	3493	|gi|1591672	|phosphate transport system ATP-binding protein |Methanococcus jannaschii|	88	68	771
160	8	5853	6278	|gi|1773267	|ATPase, epsilon subunit |Streptococcus mutans|	88	65	426
177	4	1770	2885	|gi|149426	|putative |Lactococcus lactis|	88	72	1116
211	6	4140	3613	|gi|535273	|aminopeptidase C |Streptococcus thermophilus|	88	74	528
231	4	580	957	|gi|40186	|homologous to E.coli ribosomal protein L27 |Bacillus subtilis|	88	78	378
260	5	2387	2998	|gi|1196922	|unknown protein |Insertion sequence IS861|	88	69	612
291	6	2017	3375	|gnl|PID|d100571	|adenylosuccinate synthetase |Bacillus subtilis|	88	75	1359
319	4	658	317	|gi|603578	|serine/threonine kinase |Phytophthora capsici|	88	88	342
40	5	4353	4514	|gi|153672	|lactose repressor |Streptococcus mutans|	87	56	162

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
49	10	10660	10929	gi|1196921	unknown protein (insertion sequence IS861)	87	72	270
65	7	3140	3808	gi|1165309	S3 (Bacillus subtilis)	87	73	669
65	15	6623	7039	gi|1044978	ribosomal protein S8 (Bacillus subtilis)	87	73	417
75	8	5411	6625	gi|1877422	galactokinase (Streptococcus mutans)	87	78	1215
80	2	703	2805	gnl|PID|d101166	elongation factor G (Bacillus subtilis)	87	76	2103
82	1	541	248	gi|1196921	unknown protein (insertion sequence IS861)	87	69	294
140	23	25033	23897	gnl|PID|e254999	phenylalany-tRNA synthetase beta subunit (Bacillus subtilis)	87	74	1137
214	14	10441	8516	gi|2281305	glucose inhibited division protein homolog GidA (Lactococcus lactis cremoris)	87	75	1926
220	2	2742	874	gnl|PID|e324358	product highly similar to elongation factor EF-G (Bacillus subtilis)	87	73	1869
260	4	2096	2389	gi|1196921	unknown protein (insertion sequence IS861)	87	72	294
323	1	27	650	gi|897795	30S ribosomal protein (Pediococcus acidilactici)	87	73	624
357	1	154	570	gi|1044978	ribosomal protein S8 (Bacillus subtilis)	87	73	417
49	11	10927	11445	gi|1196922	unknown protein (insertion sequence IS861)	86	63	519
59	12	7461	9224	gi|951051	relaxase (Streptococcus pneumoniae)	86	68	1764
65	4	1553	2401	pir|A02759|R5BS	ribosomal protein L2 - Bacillus stearothermophilus	86	77	849
65	23	10957	11610	gi|44074	adenylate kinase (Lactococcus lactis)	86	76	654
82	4	4374	4856	gi|153745	mannitol-specific enzyme III (Streptococcus mutans)	86	72	483
102	4	4270	4986	gnl|PID|e264705	OMP decarboxylase (Lactococcus lactis)	86	76	717
106	6	7824	6880	gnl|PID|e137598	aspartate transcarbamylase (Lactobacillus leichmannii)	86	68	945
107	1	1	273	gnl|PID|e339862	putative acylneuraminate lyase (Clostridium tertium)	86	71	273
111	7	10432	6710	gnl|PID|e22828)	DNA-dependent RNA polymerase (Streptococcus pyogenes)	86	80	3723
131	9	5704	4892	gi|1661193	polipoprotein diacylglycerol transferase (Streptococcus mutans)	86	71	813
134	7	6430	7980	gi|2388637	glycerol kinase (Enterococcus faecalis)	86	73	1551
146	11	7473	6583	gi|1591731	melvalonate kinase (Methanococcus jannaschii)	86	72	891
153	2	595	2010	gi|2160707	dipeptidase (Lactococcus lactis)	86	78	1416
154	1	2	1435	gi|1857246	6-phosphogluconate dehydrogenase (Lactococcus lactis)	86	74	1434

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
161	5	5025	6284	gi|47529	Unknown (Streptococcus salivarius)	86	66	1260
184	1	2	1483	gi|642667	NADP-dependent glyceraldehyde-3-phosphate dehydrogenase (Streptococcus mutans)	86	73	1482
210	8	3659	6571	gi|153661	translational initiation factor IF2 (Enterococcus faecium)	86	76	2913
250	1	2	187	gi|1573551	asparagine synthetase A (asnA) (Haemophilus influenzae)	86	68	186
36	4	2644	3909	gi|2149909	cell division protein (Enterococcus faecalis)	85	73	1266
38	4	2475	3587	gi|2058545	putative ABC transporter subunit ComYB (Streptococcus gordonii)	85	72	1113
38	5	3577	3915	gi|2058546	ComYC (Streptococcus gordonii)	85	80	339
57	5	2797	3789	gnl|PID|d101316	YqfJ (Bacillus subtilis)	85	72	993
82	5	4915	6054	gi|153746	mannitol-phosphate dehydrogenase (Streptococcus mutans)	85	68	1140
83	15	14690	15793	gi|143371	phosphoribosyl aminoimidazole synthetase (PUR-M) (Bacillus subtilis)	85	69	1104
87	2	1417	2388	gi|1184967	ScrR (Streptococcus mutans)	85	69	972
108	3	2666	3154	gi|153566	ORF (19K protein) (Enterococcus faecalis)	85	67	489
127	2	312	692	gi|1044989	ribosomal protein S13 (Bacillus subtilis)	85	72	381
128	3	1534	2409	gi|1685110	tetrahydrofolate dehydrogenase/cyclohydrolase (Streptococcus thermophilus)	85	71	876
137	7	2962	4767	gnl|PID|d100347	Na+ -ATPase alpha subunit (Enterococcus hirae)	85	74	1806
170	2	2622	709	gnl|PID|d102006	(AB001488) FUNCTION UNKNOWN, SIMILAR PRODUCT IN E.COLI, H. INFLUENZAE AND NEISSERIA MENINGITIDIS. (Bacillus subtilis)	85	70	1914
187	5	3760	4386	gi|727436	putative 20-kDa protein (Lactococcus lactis)	85	65	627
233	2	728	1873	gi|1163116	ORF-5 (Streptococcus pneumoniae)	85	67	1146
234	3	962	1255	gi|2293155	(AF008220) YtlA (Bacillus subtilis)	85	61	294
240	1	309	1931	gi|143597	CTP synthetase (Bacillus subtilis)	85	70	1623
6	1	199	1521	gi|508979	GTP-binding protein (Bacillus subtilis)	84	72	1323
10	4	4375	3443	gnl|PID|e339862	putative acylneuraminate lyase (Clostridium tertium)	84	70	933
14	1	63	2093	gi|520753	DNA topoisomerase I (Bacillus subtilis)	84	69	2031
19	4	1793	2593	gi|2352484	(AF005098) RNAseH II (Lactococcus lactis)	84	68	801
20	17	17720	19687	gnl|PID|d100584	cell division protein (Bacillus subtilis)	84	71	1968
22	28	21723	20884	gi|299163	alanine dehydrogenase (Bacillus subtilis)	84	68	840

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
30	10	7730	6792	gnl|PID|d100296	fructokinase [Streptococcus mutans]	84	75	939
33	9	5650	5300	gi|147194	phnA protein [Escherichia coli]	84	71	351
36	22	21551	20772	gi|310631	ATP binding protein [Streptococcus gordonii]	84	72	780
48	4	2837	2505	gi|882609	6-phospho-beta-glucosidase [Escherichia coli]	84	69	333
58	1	41	1516	gi|450849	amylase [Streptococcus bovis]	84	73	1476
59	10	6715	7116	gi|951053	ORF10, putative [Streptococcus pneumoniae]	84	74	402
62	1	21	644	gi|806487	ORF211; putative [Lactococcus lactis]	84	66	624
65	17	7779	8207	gi|1044980	ribosomal protein L18 [Bacillus subtilis]	84	73	429
65	21	9507	10397	gi|44073	SecY protein [Lactococcus lactis]	84	68	891
106	4	5474	2262	gnl|PID|e199367	carbamoyl-phosphate synthase [Lactobacillus plantarum]	84	73	3213
159	1	147	4	gi|806487	ORF211; putative [Lactococcus lactis]	84	63	144
163	4	4690	5910	gi|2293164	[AF008220] SAM synthase [Bacillus subtilis]	84	69	1221
192	1	46	1308	gi|495046	tripeptidase [Lactococcus lactis]	84	73	1263
348	1	671	6	gi|1787753	[AE000245] f346; 79 pct identical to 336 amino acids of ADH1_ZYMMO SW: P20368 but has 10 additional N-ter residues [Escherichia coli]	84	71	666
3	4	1572	3575	gi|143766	[thrSv] [EC 6.1.1.3] [Bacillus subtilis]	83	65	2004
9	6	3893	3417	gnl|PID|d100576	single strand DNA binding protein [Bacillus subtilis]	83	68	477
17	15	7426	8457	gi|520738	comA protein [Streptococcus pneumoniae]	83	66	1032
20	12	13860	14144	gnl|PID|d100583	unknown [Bacillus subtilis]	83	61	285
23	4	3358	2606	gi|1788294	[AE000290] o238; This 238 aa orf is 40 pct identical (5 gaps) to 231 residues of an approx. 248 aa protein YEBC_ECOLI SW: P24237 [Escherichia coli]	83	74	753
28	6	3304	3005	gi|1573659	H. influenzae predicted coding region HI0659 [Haemophilus influenzae]	83	57	300
35	7	5108	3867	gi|311707	hypothetical nucleotide binding protein [Acholeplasma laidlawii]	83	63	1242
55	19	17932	17528	gi|537085	ORF_f141 [Escherichia coli]	83	59	405
55	20	18539	17919	gi|496558	orfX [Bacillus subtilis]	83	69	621
65	6	2795	3142	gi|1165308	L22 [Bacillus subtilis]	83	64	348
68	6	6877	6683	gi|1213494	immunoglobulin A1 protease [Streptococcus pneumoniae]	83	54	195

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
87	15	15112	14771	gnl|PID|e323522	putative rpoZ protein [Bacillus subtilis]	83	54	342
96	12	8963	9631	gi|47394	5-oxoprolyl-peptidase [Streptococcus pyogenes]	83	73	669
98	1	3	263	gi|1183885	glutamine-binding subunit [Bacillus subtilis]	83	55	261
120	4	7170	5233	gi|310630	zinc metalloprotease [Streptococcus gordonii]	83	72	1938
127	7	2998	4347	gi|1500567	M. jannaschii predicted coding region MJ1665 [Methanococcus jannaschii]	83	72	1350
137	1	3	440	gi|472918	v-type Na-ATPase [Enterococcus hirae]	83	60	438
160	6	3466	4356	gi|1773265	ATPase, gamma subunit [Streptococcus mutans]	83	67	891
214	4	2278	2964	gi|663279	transposase [Streptococcus pneumoniae]	83	72	687
226	3	2367	2020	gi|142154	thioredoxin [Synechococcus PCC6301]	83	58	348
303	1	3	1049	gi|40046	phosphoglucose isomerase A (AA 1-449) [Bacillus stearothermophilus]	83	67	1047
303	2	1155	1931	gi|289282	glutamyl-tRNA synthetase [Bacillus subtilis]	83	67	777
6	17	15370	14318	gi|633147	ribose-phosphate pyrophosphokinase [Bacillus caldolyticus]	82	64	1053
7	1	299	96	gi|143648	ribosomal protein L28 [Bacillus subtilis]	82	69	204
9	3	1479	1090	gi|305178	unknown [Bacillus subtilis]	82	46	390
9	7	4213	3899	gnl|PID|d100576	ribosomal protein S6 [Bacillus subtilis]	82	60	315
12	6	6688	3942	gnl|PID|d100571	unknown [Bacillus subtilis]	82	68	747
22	17	13422	14837	gi|520754	putative [Bacillus subtilis]	82	69	1416
22	18	14897	15658	gnl|PID|d101929	uridine monophosphate kinase [Synechocystis sp.]	82	62	762
33	16	11471	10641	gnl|PID|d101190	ORF4 [Streptococcus mutans]	82	68	831
35	9	7400	6255	gi|1881543	UDP-N-acetylglucosamine-2-epimerase [Streptococcus pneumoniae]	82	68	1146
40	10	8003	7533	gi|1173519	riboflavin synthase beta subunit [Actinobacillus pleuropneumoniae]	82	68	471
48	32	23159	23437	gi|1930092	outer membrane protein [Campylobacter jejuni]	82	61	279
52	14	13833	14765	gi|142521	deoxyribodipyrimidine photolyase [Bacillus subtilis]	82	61	933
60	4	4737	1849	gnl|PID|d102221	(AB001610) uvrA [Deinococcus radiodurans]	82	66	2889
62	4	2131	1457	gi|2246749	(AF00962]) thioredoxin reductase [Listeria monocytogenes]	82	63	675
71	11	16586	17518	gnl|PID|e322063	ss-1,4-galactosyltransferase [Streptococcus pneumoniae]	82	60	933
73	13	9222	7837	gnl|PID|d100586	unknown [Bacillus subtilis]	82	65	1386

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
74	1	1	3771	gnl|PID|d101199	alkaline amylopullulanase (Bacillus sp.)	82	68	3771
83	9	3696	3983	gnl|PID|e305362	unnamed protein product (Streptococcus thermophilus)	82	52	288
86	11	10776	9394	gi|683583	5-enolpyruvylshikimate-3-phosphate synthase (Lactococcus lactis)	82	67	1383
89	12	8295	9752	gi|40025	homologous to E.coli 50K (Bacillus subtilis)	82	66	1458
115	9	10347	8812	gnl|PID|d102090	(AB003927) phospho-beta-galactosidase 1 (Lactobacillus gasseri)	82	74	1536
118	1	1	1332	gnl|PID|d100579	seryl-tRNA synthetase (Bacillus subtilis)	82	71	1332
151	3	4657	6246	pir|S06097|S060	type I site-specific deoxyribonuclease (EC 3.1.21.3) CfrA chain S - Citrobacter freundii	82	66	1590
173	6	4183	3503	gi|2313836	(AE000584) conserved hypothetical protein (Helicobacter pylori)	82	68	681
177	12	5481	7442	gnl|PID|d101999	(AB001341) NcrB (Escherichia coli)	82	58	1962
193	2	178	576	pir|S08564|RJBS	ribosomal protein S9 - Bacillus stearothermophilus	82	70	399
245	2	258	845	gi|146402	EcoA type I restriction-modification enzyme S subunit (Escherichia coli)	82	68	588
9	5	3400	3146	gnl|PID|d100576	ribosomal protein S18 (Bacillus subtilis)	81	66	255
16	7	7484	8413	gi|1100074	tryptophanyl-tRNA synthetase (Clostridium longisporum)	81	70	930
20	11	10308	13820	gnl|PID|d100583	transcription-repair coupling factor (Bacillus subtilis)	81	63	3513
38	2	1232	1606	gi|2058543	putative DNA binding protein (Streptococcus gordonii)	81	63	375
45	2	3061	1751	gi|460259	enolase (Bacillus subtilis)	81	67	1311
46	1	2	1267	gi|431231	uracil permease (Bacillus caldolyticus)	81	61	1266
48	3	2453	1440	gnl|PID|d100453	Mannosephosphate isomerase (Streptococcus mutans)	81	70	1014
54	2	1106	336	gi|154752	transport protein (Agrobacterium tumefaciens)	81	64	771
65	22	10306	10821	gi|44073	SecY protein (Lactococcus lactis)	81	66	516
89	4	3874	2603	gi|556886	serine hydroxymethyltransferase (Bacillus subtilis)	81	69	1272
99	16	19126	18929	gi|2313526	(AE000557) H. pylori predicted coding region HP0411 (Helicobacter pylori)	81	75	198
106	7	8373	7822	gnl|PID|e199384	pyrR (Lactobacillus plantarum)	81	61	552
108	6	5054	6877	gi|1469939	group B oligopeptidase PepB (Streptococcus agalactiae)	81	66	1824
113	15	15899	18283	pir|S09411|S094	spoIIIE protein - Bacillus subtilis	81	65	2385
128	5	3359	3634	gi|1685111	orf1091 (Streptococcus thermophilus)	81	69	276

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match accession	match gene name	% sim	% ident	length (nt)
151	1	830	3211	|gi|304896	|EcoE type I restriction-modification enzyme R subunit (Escherichia coli)	81	59	2382
159	11	6722	7837	|gi|2239288	|GMP synthetase (Bacillus subtilis)	81	69	1116
170	1	739	458	|gnl|PID|d102006	|(AB001488) FUNCTION UNKNOWN. (Bacillus subtilis)	81	55	282
191	2	1759	893	|gi|149522	|tryptophan synthase alpha subunit (Lactococcus lactis)	81	65	867
214	3	2290	1994	|gi|157587	|reverse transcriptase endonuclease (Drosophila virilis)	81	63	297
217	4	4415	4008	|gi|466473	|cellobiose phosphotransferase enzyme II' (Bacillus stearothermophilus)	81	59	408
262	2	569	868	|gi|153675	|tagatose 6-P kinase (Streptococcus mutans)	81	68	300
299	1	663	4	|gnl|PID|e301154	|StySKI methylase (Salmonella enterica)	81	60	660
366	2	376	83	|gi|149521	|tryptophan synthase beta subunit (Lactococcus lactis)	81	65	294
12	10	8766	9242	|gi|1216490	|DNA/pantothenate metabolism flavoprotein (Streptococcus mutans)	80	64	477
17	11	6050	5748	|gnl|PID|e305362	|unnamed protein product (Streptococcus thermophilus)	80	67	303
17	16	8455	9066	|gi|703126	|leucocin A translocator (Leuconostoc gelidum)	80	59	612
18	3	2440	1613	|gi|1591672	|phosphate transport system ATP-binding protein (Methanococcus jannaschii)	80	58	828
27	3	4248	1579	|gi|452309	|valyl-tRNA synthetase (Bacillus subtilis)	80	69	2670
28	7	3671	3288	|gi|1573660	|H. influenzae predicted coding region HI0660 (Haemophilus influenzae)	80	63	384
32	2	902	1933	|gnl|PID|e264499	|dihydroorotate dehydrogenase B (Lactococcus lactis)	80	66	1032
39	1	1	1266	|gnl|PID|e234078	|hom (Lactococcus lactis)	80	63	1266
52	5	4363	3593	|gi|1183884	|ATP-binding subunit (Bacillus subtilis)	80	57	771
54	5	4550	4744	|gi|2198820	|(AF004225) Cux/CDP(1B1); Cux/CDP homeoprotein (Mus musculus)	80	60	195
59	11	7109	7486	|gi|951052	|ORF9, putative (Streptococcus pneumoniae)	80	68	378
65	3	1230	1550	|pir|A02815|R5BS	|ribosomal protein L23 - Bacillus stearothermophilus	80	69	321
65	12	5174	5503	|pir|A02819|R5BS	|ribosomal protein L24 - Bacillus stearothermophilus	80	70	330
66	9	9884	10687	|gi|2313836	|(AE000584) conserved hypothetical protein (Helicobacter pylori)	80	66	804
82	2	648	243R	|gi|622991	|mannitol transport protein (Bacillus stearothermophilus)	80	65	1791
85	1	950	630	|gi|528995	|polyketide synthase (Bacillus subtilis)	80	46	321
89	8	6870	5779	|gi|853776	|peptide chain release factor 1 (Bacillus subtilis)	80	63	1092
93	12	8718	7438	|gnl|PID|d101959	|hypothetical protein (Synechocystis sp.)	80	60	1281

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
106	5	6854	5751	gnl|PID|e199386	glutaminase of carbamoyl-phosphate synthase (Lactobacillus plantarum)	80	65	1104
109	2	2160	1450	gi|40056	phoP gene product (Bacillus subtilis)	80	59	711
124	9	4246	3953	gnl|PID|d102254	30S ribosomal protein S16 (Bacillus subtilis)	80	65	294
128	8	5148	6428	gi|2281308	phosphopentomutase (Lactococcus lactis cremoris)	80	66	1281
137	19	12665	11376	gi|159109	NADP-dependent glutamate dehydrogenase (Giardia intestinalis)	80	68	1290
140	19	19699	19457	gi|517210	putative transposase (Streptococcus pyogenes)	80	70	243
158	2	2474	984	gi|1077423	galactose-1-P-uridyl transferase (Streptococcus mutans)	80	65	1491
171	10	7474	7728	gi|397800	cyclophilin C-associated protein (Mus musculus)	80	60	255
181	1	2	619	gi|149395	lacC (Lactococcus lactis)	80	66	618
313	1	27	539	gi|143467	ribosomal protein S4 (Bacillus subtilis)	80	70	513
329	2	1652	858	gi|533080	RecF protein (Streptococcus pyogenes)	80	63	795
371	1	2	958	gi|442360	ClpC adenosine triphosphatase (Bacillus subtilis)	80	58	957
8	7	4312	5580	gi|149435	putative (Lactococcus lactis)	79	64	1269
23	1	1175	135	gi|1542975	AbcB (Thermoanaerobacterium thermosulfurigenes)	79	61	1041
33	14	9244	8201	gnl|PID|e253891	UDP-glucose 4-epimerase (Bacillus subtilis)	79	62	1044
36	3	1242	2633	gnl|PID|e324218	ftsA (Enterococcus hirae)	79	58	1392
38	13	7155	8378	gi|405134	acetate kinase (Bacillus subtilis)	79	58	1224
55	7	9011	8229	gi|1146234	dihydrodipicolinate reductase (Bacillus subtilis)	79	56	783
65	19	8661	8915	gi|2078380	ribosomal protein L30 (Staphylococcus aureus)	79	68	255
69	4	3678	2128	gnl|PID|e311452	unknown (Bacillus subtilis)	79	64	1551
69	9	7881	7279	gi|677850	hypothetical protein (Staphylococcus aureus)	79	59	603
72	10	8491	9783	gnl|PID|d101091	hypothetical protein (Synechocystis sp.)	79	62	1293
80	3	2906	7300	gi|143342	polymerase III (Bacillus subtilis)	79	65	4395
82	14	13326	15689	gnl|PID|e255093	hypothetical protein (Bacillus subtilis)	79	65	2364
86	13	12213	11118	gi|683582	prephenate dehydrogenase (Lactococcus lactis)	79	58	1116
92	3	940	1734	gi|537286	triosephosphate isomerase (Lactococcus lactis)	79	65	795
98	6	4023	4742	gnl|PID|d100262	LivG protein (Salmonella typhimurium)	79	63	720

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match accession	match gene name	% sim	% ident	length (nt)
99	12	16315	14150	gi|153736	a-galactosidase (Streptococcus mutans)	79	64	2166
107	7	5684	6406	gi|460080	D-alanine:D-alanine ligase-related protein (Enterococcus faecalis)	79	58	723
113	9	6858	8303	gi|466882	ppsI; B1496_C2_189 (Mycobacterium leprae)	79	64	1446
151	10	13424	12213	gi|450686	3-phosphoglycerate kinase (Thermotoga maritima)	79	60	1212
162	2	1158	3017	gi|506700	CapD (Staphylococcus aureus)	79	67	1860
177	5	2876	3052	gi|912423	putative (Lactococcus lactis)	79	61	177
177	8	4198	4563	gi|149429	putative (Lactococcus lactis)	79	61	366
187	3	2728	2907	gnl|PID|d102002	(AB0001488) FUNCTION UNKNOWN. (Bacillus subtilis)	79	53	180
189	7	3589	4350	gnl|PID|e183449	putative ATP-binding protein of ABC-type (Bacillus subtilis)	79	61	762
191	5	4249	3449	gi|149519	indoleglycerol phosphate synthase (Lactococcus lactis)	79	66	801
211	3	1805	2737	gi|147404	mannose permease subunit II-M-Man (Escherichia coli)	79	57	933
212	3	3863	3621	gnl|PID|e209004	glutaredoxin-like protein (Lactococcus lactis)	79	58	243
215	1	987	715	gi|2293242	(AF008220) arginine succinate synthase (Bacillus subtilis)	79	64	273
323	2	530	781	gi|897795	30S ribosomal protein (Pediococcus acidilactici)	79	67	252
380	1	694	2	gi|1184680	polynucleotide phosphorylase (Bacillus subtilis)	79	64	693
384	2	655	239	gi|143328	phoP protein (put.); putative (Bacillus subtilis)	79	59	417
6	3	2820	4091	gi|853767	UDP-N-acetylglucosamine 1-carboxyvinyltransferase (Bacillus subtilis)	78	62	1272
8	1	50	1786	gi|149432	putative (Lactococcus lactis)	78	63	1737
9	1	351	124	gi|897793	y98 gene product (Pediococcus acidilactici)	78	59	228
15	8	7364	8314	gnl|PID|d100585	cysteine synthetase A (Bacillus subtilis)	78	63	951
20	10	9738	10310	gnl|PID|d100583	stage V sporulation (Bacillus subtilis)	78	58	573
20	16	17165	17713	gi|49105	hypoxanthine phosphoribosyltransferase (Lactococcus lactis)	78	59	549
22	22	17388	18416	gnl|PID|d101315	YqfE (Bacillus subtilis)	78	60	1029
22	27	20971	20612	gi|299163	alanine dehydrogenase (Bacillus subtilis)	78	59	360
34	8	7407	7105	gi|41015	aspartate-tRNA ligase (Escherichia coli)	78	55	303
35	8	6257	5196	gi|1657644	Cap8E (Staphylococcus aureus)	78	60	1062

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
40	11	9287	8001	gi|1173518	GTP cyclohydrase II/ 3,4-dihydroxy-2-butanone-4-phosphate synthase [Actinobacillus pleuropneumoniae]	78	58	1287
48	31	22422	23183	gi|2314330	(AE000623) glutamine ABC transporter, ATP-binding protein (glnQ) [Helicobacter pylori]	78	58	762
52	2	2101	1430	gi|1183887	integral membrane protein [Bacillus subtilis]	78	54	672
55	14	13605	12712	gnl|PID|d102026	(AB002150) YbbP [Bacillus subtilis]	78	58	894
55	17	16637	15612	gnl|PID|e313027	hypothetical protein [Bacillus subtilis]	78	51	1026
71	14	19756	19598	gi|179764	calcium channel alpha-1D subunit [Homo sapiens]	78	57	159
74	11	15031	14018	gi|1573279	Holliday junction DNA helicase (ruvB) [Haemophilus influenzae]	78	57	1014
75	9	6623	7972	gi|1877423	galactose-1-P-uridyl transferase [Streptococcus mutans]	78	62	1350
81	12	12125	13906	gi|1573607	L-fucose isomerase (fucI) [Haemophilus influenzae]	78	66	1782
82	3	2423	4417	gi|153744	ORF X; putative [Streptococcus mutans]	78	64	1995
83	18	16926	18500	gi|143373	phosphoribosyl aminoimidazole carboxy formyl formyltransferase/inosine monophosphate cyclohydrolase (PUR-H(J)) [Bacillus subtilis]	78	63	1575
83	20	20212	20775	gi|143364	phosphoribosyl aminoimidazole carboxylase I (PUR-E) [Bacillus subtilis]	78	64	564
92	2	165	878	gnl|PID|d101190	ORF2 [Streptococcus mutans]	78	62	714
98	8	5863	6909	gi|2331287	(AF013188) release factor 2 [Bacillus subtilis]	78	63	1047
113	3	1071	2741	gi|580914	dnaZX [Bacillus subtilis]	78	64	1671
127	4	1133	2071	gi|142463	RNA polymerase alpha-core-subunit [Bacillus subtilis]	78	59	939
132	1	2782	497	gi|1561763	pullulanase [Bacteroides thetaiotaomicron]	78	58	2286
135	4	2698	3537	gi|1788036	(AE000269) NH3-dependent NAD synthetase [Escherichia coli]	78	66	840
140	24	26853	25423	gi|1100077	phospho-beta-glucosidase [Clostridium longisporum]	78	64	1431
150	5	4690	4514	gi|149464	amino peptidase [Lactococcus lactis]	78	42	177
152	1	1	795	gi|639915	NADH dehydrogenase subunit [Thunbergia alata]	78	43	795
162	4	4997	4110	gnl|PID|e323528	putative YhaP protein [Bacillus subtilis]	78	64	888
181	10	8651	7947	gi|149402	lactose repressor (lacR; alt.) [Lactococcus lactis]	78	48	705
200	4	3627	4958	gnl|PID|d100172	invertase [Zymomonas mobilis]	78	61	1332
203	3	3230	3015	gi|1174237	CycK [Pseudomonas fluorescens]	78	57	216

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
210	9	6789	7172	gi|580902	ORF6 gene product (Bacillus subtilis)	78	62	384
214	6	3810	2797	gnl|PID|d102049	P. haemolytica o-sialoglycoprotein endopeptidase; PJ6175 (660) transmembrane (Bacillus subtilis)	78	60	1014
214	13	6322	8163	gi|1377831	unknown (Bacillus subtilis)	78	62	1842
217	1	9	2717	gi|488430	alcohol dehydrogenase 2 (Entamoeba histolytica)	78	64	2709
222	3	2316	3098	gi|1573047	spore germination and vegetative growth protein (gerC2) (Haemophilus influenzae)	78	65	783
268	1	742	8	gi|517210	putative transposase (Streptococcus pyogenes)	78	65	735
276	1	223	753	gnl|PID|d100306	ribosomal protein L1 (Bacillus subtilis)	78	65	531
312	3	1567	1079	gi|289261	comE ORF2 (Bacillus subtilis)	78	54	489
339	1	117	794	gi|1916729	CadD (Staphylococcus aureus)	78	53	678
342	2	762	265	gi|1842439	phosphatidylglycerophosphate synthase (Bacillus subtilis)	78	59	498
383	1	737	3	gi|1184680	polynucleotide phosphorylase (Bacillus subtilis)	78	64	735
7	15	11923	11018	gi|1399855	carboxyltransferase beta subunit (Synechococcus PCC7942)	77	63	906
8	2	1698	2255	gi|149433	putative (Lactococcus lactis)	77	59	558
17	14	6948	7550	gi|520738	comA protein (Streptococcus pneumoniae)	77	60	603
30	12	9761	8967	gi|1000451	TreP (Bacillus subtilis)	77	43	795
36	14	11421	12131	gi|1573766	phosphoglyceromutase (gpmA) (Haemophilus influenzae)	77	64	711
55	3	3836	4096	gi|1708640	YeaB (Bacillus subtilis)	77	55	261
61	8	8377	8054	gi|1890649	multidrug resistance protein LmrA (Lactococcus lactis)	77	51	324
65	2	607	1254	gi|40103	ribosomal protein L4 (Bacillus stearothermophilus)	77	63	648
68	8	7509	7240	gi|47551	MRP (Streptococcus suis)	77	68	270
69	1	1083	118	gnl|PID|e311493	unknown (Bacillus subtilis)	77	57	966
77	5	4583	4026	gnl|PID|e281578	hypothetical 12.2 kd protein (Bacillus subtilis)	77	60	558
83	14	13104	14552	gi|1590947	amidophosphoribosyltransferase (Methanococcus jannaschii)	77	56	1449
94	4	3006	5444	gnl|PID|e329895	(AJ000496) cyclic nucleotide-gated channel beta subunit (Rattus norvegicus)	77	66	2439
96	11	8518	8880	gi|551879	ORF 1 (Lactococcus lactis)	77	62	363
99	11	14082	12799	gi|153737	sugar-binding protein (Streptococcus mutans)	77	61	1284

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match accession	match gene name	% sim	% ident	length (nt)
106	2	361	1176	gi|148921	LicD protein (Haemophilus influenzae)	77	51	816
108	4	3152	4030	gi|1574730	tellurite resistance protein (tehB) (Haemophilus influenzae)	77	58	879
118	4	3520	3131	gi|1573900	D-alanine permease (dagA) (Haemophilus influenzae)	77	57	390
124	4	1796	1071	gi|1573162	tRNA (guanine-N1)-methyltransferase (trmD) (Haemophilus influenzae)	77	58	726
126	4	5909	4614	gnl|PID|d101163	Srb (Bacillus subtilis)	77	62	1296
128	2	630	1373	gnl|PID|d101328	YqiZ (Bacillus subtilis)	77	58	744
130	1	1	1287	gnl|PID|e325013	hypothetical protein (Bacillus subtilis)	77	61	1287
139	5	4388	3639	gi|2293302	(AF008220) YtqA (Bacillus subtilis)	77	59	750
140	11	10931	9582	gi|289284	cysteinyl-tRNA synthetase (Bacillus subtilis)	77	64	1350
140	18	19451	19263	gi|517210	putative transposase (Streptococcus pyogenes)	77	66	189
141	2	976	1683	gnl|PID|e157887	URF5 (aa 1-573) (Drosophila yakuba)	77	50	708
141	4	2735	5293	gi|556258	secA (Listeria monocytogenes)	77	59	2559
144	2	671	2173	gnl|PID|d100585	lysyl-tRNA thynthetase (Bacillus subtilis)	77	61	1503
163	5	6412	7398	gi|511015	dihydroorotate dehydrogenase A (Lactococcus lactis)	77	62	987
164	10	7841	7074	gnl|PID|d100964	homologue of iron dicitrate transport ATP-binding protein FecE of E. coli (Bacillus subtilis)	77	52	768
191	8	7257	5791	gi|149516	anthranilate synthase alpha subunit (Lactococcus lactis)	77	57	1467
198	8	5377	5177	gi|1573856	hypothetical (Haemophilus influenzae)	77	66	201
213	1	202	462	gi|1743860	Brca2 (Mus musculus)	77	50	261
250	2	231	509	gnl|PID|e334776	YlbH protein (Bacillus subtilis)	77	60	279
289	3	1737	1276	gnl|PID|d100947	Ribosomal Protein L10 (Bacillus subtilis)	77	62	462
292	2	1399	668	gi|143004	transfer RNA-Gln synthetase (Bacillus stearothermophilus)	77	58	732
7	3	2734	1166	gnl|PID|d101824	peptide-chain-release factor 3 (Synechocystis sp.)	76	53	1569
7	23	18474	18235	gi|455157	acyl carrier protein (Cryptomonas phi)	76	57	240
9	8	5706	4342	gi|1146247	asparaginyl-tRNA synthetase (Bacillus subtilis)	76	61	1365
10	5	4531	4185	gnl|PID|e314495	hypothetical protein (Clostridium perfringens)	76	53	147
18	2	1615	842	gi|1591672	phosphate transport system ATP-binding protein (Methanococcus jannaschii)	76	56	774

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
22	37	27796	28173	gnl|PID|e133B9	translation initiation factor IF3 (AA 1-172) [Bacillus stearothermophilus]	76	64	378
35	6	3869	2682	gi|1773346	CapSG [Staphylococcus aureus]	76	61	1188
48	28	21113	21787	gi|2314328	(AE000623) glutamine ABC transporter, permease protein (glnP) [Helicobacter pylori]	76	52	675
52	12	12881	13786	gi|142521	deoxyribodipyrimidine photolyase [Bacillus subtilis]	76	58	906
55	10	11521	10571	gnl|PID|e283110	femD [Staphylococcus aureus]	76	61	951
57	8	7824	6559	gi|290561	o188 [Escherichia coli]	76	47	1266
62	5	2406	2095	gnl|PID|e313024	hypothetical protein [Bacillus subtilis]	76	59	312
65	9	4223	4441	gi|40148	L29 protein (AA 1-66) [Bacillus subtilis]	76	58	219
68	2	1328	2371	gnl|PID|e284233	anabolic ornithine carbamoyltransferase [Lactobacillus plantarum]	76	61	1044
69	8	7297	6005	gnl|PID|d101420	Pyrimidine nucleoside phosphorylase [Bacillus stearothermophilus]	76	61	1293
73	12	7839	7267	gnl|PID|e243629	unknown [Mycobacterium tuberculosis]	76	53	573
74	5	8433	7039	gnl|PID|d102048	C. thermocellum beta-glucosidase; P26208 (985) [Bacillus subtilis]	76	60	1395
80	5	7643	7936	gi|2314030	(AE000599) conserved hypothetical protein [Helicobacter pylori]	76	61	294
82	15	16019	16996	gi|1573900	D-alanine permease (dagA) [Haemophilus influenzae]	76	56	978
83	19	18616	19884	gi|143374	phosphoribosyl glycinamide synthetase (PUR-D; gtg start codon) [Bacillus subtilis]	76	60	1269
86	14	13409	12231	gi|143806	AroF [Bacillus subtilis]	76	58	1179
87	1	1	1442	gi|153804	sucrose-6-phosphate hydrolase [Streptococcus mutans]	76	59	1440
87	16	15754	15110	gnl|PID|e323500	putative Gmk protein [Bacillus subtilis]	76	56	645
93	4	1769	1539	gi|1574820	1,4-alpha-glucan branching enzyme (glgB) [Haemophilus influenzae]	76	46	231
94	1	51	365	gi|144313	6.0 kd ORF [Plasmid ColE1]	76	73	315
116	2	2151	1678	gi|153841	pneumococcal surface protein A [Streptococcus pneumoniae]	76	59	474
123	6	3442	5895	gi|1314297	ClpC ATPase [Listeria monocytogenes]	76	59	2454
126	2	2156	2932	gnl|PID|d101328	YqiZ [Bacillus subtilis]	76	61	777
128	10	6973	7797	gi|944944	purine nucleoside phosphorylase [Bacillus subtilis]	76	60	825
131	11	6186	5812	gi|1674310	(AE000058) Mycoplasma pneumoniae, MG085 homolog, from M. genitalium [Mycoplasma pneumoniae]	76	47	375

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
139	4	3641	3192	gi|2293302	(AF008220) YtqA (Bacillus subtilis)	76	53	450
140	14	14872	12536	gi|1184680	polynucleotide phosphorylase (Bacillus subtilis)	76	62	2337
143	2	2583	3905	gi|143795	transfer RNA-Tyr synthetase (Bacillus subtilis)	76	61	1323
170	6	5095	6114	gnl|PID|d100959	ycgQ (Bacillus subtilis)	76	44	1020
180	2	1927	557	gi|40019	ORF 821 (aa 1-821) (Bacillus subtilis)	76	53	1371
191	7	5815	5228	gi|551880	anthranilate synthase beta subunit (Lactococcus lactis)	76	61	588
195	3	3829	2444	gi|2149905	D-glutamic acid adding enzyme (Enterococcus faecalis)	76	60	1386
200	3	1914	3629	gi|431272	lysis protein (Bacillus subtilis)	76	58	1716
201	1	431	207	gi|2208998	dextran glucosidase DexS (Streptococcus suis)	76	57	225
214	2	1283	2380	gi|663278	transposase (Streptococcus pneumoniae)	76	55	1098
225	3	2338	3411	gi|1552775	ATP-binding protein (Escherichia coli)	76	56	1074
233	1	2	724	gi|1163115	neuraminidase B (Streptococcus pneumoniae)	76	60	723
347	1	523	38	gi|537033	ORF_f356 (Escherichia coli)	76	60	486
356	2	842	165	gi|2149905	D-glutamic acid adding enzyme (Enterococcus faecalis)	76	61	678
366	3	734	348	gi|149520	phosphoribosyl anthranilate isomerase (Lactococcus lactis)	76	69	387
5	8	12599	11484	gi|1574293	fimbrial transcription regulation repressor (pilB) (Haemophilus influenzae)	75	6	1116
6	13	12553	11894	gnl|PID|d102050	ydiH (Bacillus subtilis)	75	51	660
9	10	7282	6062	gi|142538	aspartate aminotransferase (Bacillus sp.)	75	55	1221
10	12	8080	7940	gi|149493	SCRFI methylase (Lactococcus lactis)	75	56	141
18	5	4266	3301	gnl|PID|d101319	YqgH (Bacillus subtilis)	75	52	966
22	4	1838	2728	gi|1373157	orf-X; hypothetical protein; Method: conceptual translation supplied by author (Bacillus subtilis)	75	62	891
30	11	9015	7828	gi|153801	enzyme scr-II (Streptococcus mutans)	75	64	1188
31	5	2362	2030	gi|2293211	(AF008220) putative thioredoxin (Bacillus subtilis)	75	53	333
32	9	7484	8359	gnl|PID|d100560	formamidopyrimidine-DNA glycosylase (Streptococcus mutans)	75	61	876
33	4	1735	1448	gi|413976	ipa-52r gene product (Bacillus subtilis)	75	53	288
33	10	6470	5769	gi|533105	unknown (Bacillus subtilis)	75	56	702

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known prpteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
33	12	6878	7183	pir|A00205|FECL	ferredoxin (4Fe-4S) - Clostridium thermaceticum	75	56	306
36	1	181	2	gi|2088739	(AF003141) strong similarity to the FABP/P2/CRBP/CRABP family of transporters (Caenorhabditis elegans)	75	43	180
38	22	14510	15379	gi|1574058	hypothetical (Haemophilus influenzae)	75	56	870
48	33	23398	24066	gi|1930092	outer membrane protein (Campylobacter jejuni)	75	56	669
51	1	2	319	gi|43985	nifS-like gene (Lactobacillus delbrueckii)	75	55	318
51	10	8318	11683	gi|537192	CG Site No. 620; alternate gene names hs, hsp, hsr, rmx apparent frameshift in GenBank Accession Number X06545 (Escherichia coli)	75	50	3366
54	18	19566	20759	gi|666069	orf2 gene product (Lactobacillus leichmannii)	75	58	1194
57	9	8448	7822	gi|290561	o188 (Escherichia coli)	75	50	627
65	14	6072	6356	gi|606241	30S ribosomal subunit protein S14 (Escherichia coli)	75	64	285
70	4	3071	2472	gi|1256617	adenine phosphoribosyltransferase (Bacillus subtilis)	75	57	600
71	24	30399	29404	gi|1574390	C4-dicarboxylate transport protein (Haemophilus influenzae)	75	57	996
73	2	910	455	gnl|PID|e249656	YneT (Bacillus subtilis)	75	57	456
79	1	1810	491	gi|1146219	28.2% of identity to the Escherichia coli GTP-binding protein Era; putative (Bacillus subtilis)	75	59	1320
82	6	6360	6536	gi|1655715	BztD (Rhodobacter capsulatus)	75	55	177
83	6	1938	2975	gnl|PID|e323529	putative PlsX protein (Bacillus subtilis)	75	56	1038
93	11	7368	5317	gi|39989	methionyl-tRNA synthetase (Bacillus stearothermophilus)	75	58	2052
93	13	9409	8699	gi|1591493	glutamine transport ATP-binding protein Q (Methanococcus jannaschii)	75	54	711
95	1	1795	47	gnl|PID|e323510	YloV protein (Bacillus subtilis)	75	57	1749
103	2	362	1186	gnl|PID|e266928	unknown (Mycobacterium tuberculosis)	75	64	825
104	1	691	915	gi|460026	repressor protein (Streptococcus pneumoniae)	75	54	225
113	5	2951	3883	gnl|PID|d101119	ABC transporter subunit (Synechocystis sp.)	75	55	933
121	1	320	1390	gi|2145131	repressor of class I heat shock gene expression HrcA (Streptococcus mutans)	75	58	1071
127	6	2614	3000	gi|1500451	M. jannaschii predicted coding region MJ1558 (Methanococcus jannaschii)	75	44	387
137	18	10082	10687	gi|393116	P-glycoprotein 5 (Entamoeba histolytica)	75	52	606
149	11	8499	9338	gnl|PID|d100582	unknown (Bacillus subtilis)	75	55	840

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match accession	match gene name	% sim	% ident	length (nt)
151	6	9100	7673	gi|40467	HsdS polypeptide, part of CfrA family (Citrobacter freundii)	75	57	1428
158	1	986	3	gnl|PID|e253891	UDP-glucose 4-epimerase (Bacillus subtilis)	75	63	984
172	8	5653	6774	gi|142978	glycerol dehydrogenase (Bacillus stearothermophilus)	75	56	1122
172	9	7139	9730	gnl|PID|e268456	unknown (Mycobacterium tuberculosis)	75	58	2592
173	1	261	79	gnl|PID|e236469	C10C5.6 (Caenorhabditis elegans)	75	50	183
185	3	3066	2014	gi|1574806	spermidine/putrescine transport ATP-binding protein (potA) (Haemophilus influenzae)	75	56	1053
191	6	5235	4213	gi|149518	phosphoribosyl anthranilate transferase (Lactococcus lactis)	75	61	1023
226	2	1774	1181	gi|2314588	(AE000642) conserved hypothetical protein (Helicobacter pylori)	75	65	594
231	1	1	153	gi|40173	homolog of E.coli ribosomal protein L21 (Bacillus subtilis)	75	57	153
234	1	2	418	gi|2293259	(AF008220) YtqI (Bacillus subtilis)	75	59	417
279	1	552	151	gi|1119198	unknown protein (Bacillus subtilis)	75	50	402
291	7	3558	3827	gi|40011	ORF17 (AA 1-161) (Bacillus subtilis)	75	48	270
375	2	137	628	gi|410137	ORFX1) (Bacillus subtilis)	75	58	492
6	20	16721	17560	gi|2293323	(AF008220) YtdI (Bacillus subtilis)	74	53	840
7	6	4682	6052	gi|1354211	PET112-like protein (Bacillus subtilis)	74	60	1371
18	4	3141	2427	gnl|PID|d101319	YqgI (Bacillus subtilis)	74	54	915
21	6	5885	4800	gi|1072381	glutamyl-aminopeptidase (Lactococcus lactis)	74	59	1086
24	2	739	548	gi|2314762	(AE000655) ABC transporter, permease protein (yseE) (Helicobacter pylori)	74	46	192
25	1	2	367	gnl|PID|d100912	H2O-forming NADH Oxidase (Streptococcus mutans)	74	63	366
38	18	11432	12964	gi|537034	ORF_o488 (Escherichia coli)	74	57	1533
48	10	8924	6669	gi|1513069	P-type adenosine triphosphatase (Listeria monocytogenes)	74	53	2256
55	11	11964	11401	gnl|PID|e283110	femD (Staphylococcus aureus)	74	64	564
61	2	1782	427	gi|2293216	(AF008220) putative UDP-N-acetylmuramate-alanine ligase (Bacillus subtilis)	74	55	1356
76	10	9414	8065	gnl|PID|d101325	YqiB (Bacillus subtilis)	74	54	1350
83	2	666	926	pir|C33496|C33496	hisC homolog - Bacillus subtilis	74	55	261
86	9	8985	8080	gi|683585	prephenate dehydratase (Lactococcus lactis)	74	55	906

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
102	5	5005	5652	gi|143394	OMP-PRPP transferase (Bacillus subtilis)	74	57	648
103	5	4364	3267	gnl|PID|e323524	YloN protein (Bacillus subtilis)	74	62	1098
108	7	6864	7592	gnl|PID|e257631	methyltransferase (Lactococcus lactis)	74	56	729
131	2	478	146	gnl|PID|d101320	YqgZ (Bacillus subtilis)	74	45	333
133	2	1380	919	gnl|PID|e313025	hypothetical protein (Bacillus subtilis)	74	60	462
137	9	6167	6787	gnl|PID|d100479	Na+ -ATPase subunit D (Enterococcus hirae)	74	53	621
149	4	3008	3883	gnl|PID|d100581	high level kasgamycin resistance (Bacillus subtilis)	74	55	876
157	2	243	824	gi|1573373	methylated-DNA--protein-cysteine methyltransferase (dat1) (Haemophilus influenzae)	74	48	582
164	6	3515	4249	gi|410131	ORFX7 (Bacillus subtilis)	74	48	735
167	7	5446	5201	gi|413927	lpa-3r gene product (Bacillus subtilis)	74	55	246
171	1	1	1818	gnl|PID|d102251	beta-galactosidase (Bacillus circulans)	74	62	1818
172	4	1064	2392	gi|466474	cellobiose phosphotransferase enzyme II'' (Bacillus stearothermophilus)	74	50	1329
185	1	326	3	gi|1573646	Mg(2+) transport ATPase protein C (mgtC) (SP:P22037) (Haemophilus influenzae)	74	68	324
188	2	1089	2018	gi|1573008	ATP dependent translocator homolog (msbA) (Haemophilus influenzae)	74	44	930
189	11	6491	7174	gi|1661199	sakacin A production response regulator (Streptococcus mutans)	74	60	684
210	2	520	1287	gi|2293207	(AF008220) YtmQ (Bacillus subtilis)	74	60	768
261	1	836	192	gi|666983	putative ATP binding subunit (Bacillus subtilis)	74	55	645
263	3	1619	3655	gi|663232	Similarity with S. cerevisiae hypothetical 137.7 kD protein in subtelomeric Y' repeat region (Saccharomyces cerevisiae)	74	42	2037
265	2	844	1227	gi|49272	Asparaginase (Bacillus licheniformis)	74	64	384
360	1	1	942	gi|603998	unknown (Saccharomyces cerevisiae)	74	39	942
7	16	13357	11921	gnl|PID|d101324	YqhX (Bacillus subtilis)	73	57	1437
17	10	5706	5449	gnl|PID|e305362	unnamed protein product (Streptococcus thermophilus)	73	47	258
31	2	522	244	gnl|PID|d100576	single strand DNA binding protein (Bacillus subtilis)	73	55	279
32	6	5667	6194	gnl|PID|d101315	YqfG (Bacillus subtilis)	73	58	528
34	15	10281	9790	gnl|PID|d102151	(AB001684) ORF42c (Chlorella vulgaris)	73	46	492

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
40	12	9876	9226	gi|1173517	riboflavin synthase alpha subunit (Actinobacillus pleuropneumoniae)	73	55	651
55	2	3592	839	gnl|PID|d101887	cation-transporting ATPase PacL (Synechocystis sp.)	73	60	2754
55	18	17494	16586	gnl|PID|e265580	unknown (Mycobacterium tuberculosis)	73	52	909
65	16	7213	7767	gi|143419	ribosomal protein L6 (Bacillus stearothermophilus)	73	60	555
66	3	3300	3659	gnl|PID|e269083	LacF (Lactobacillus casei)	73	52	360
70	10	5557	5733	gi|857631	envelope protein (Human immunodeficiency virus type 1)	73	60	177
71	4	6133	8262	gnl|PID|e322063	ss-1,4-galactosyltransferase (Streptococcus pneumoniae)	73	45	2130
72	1	3	851	gi|2293177	(AF008220) transporter (Bacillus subtilis)	73	50	849
76	7	7019	6195	gnl|PID|d101325	YqiF (Bacillus subtilis)	73	66	825
76	12	10009	9533	gi|1573086	uridine kinase (uridine monophosphokinase) (udk) (Haemophilus influenzae)	73	54	477
80	7	8113	9372	gi|1177823	aminopeptidase (Bacillus subtilis)	73	60	1260
97	5	3389	1668	gnl|PID|d101954	dihydroxyacid dehydratase (Synechocystis sp.)	73	54	1722
98	9	6912	7619	gnl|PID|e314991	FtsE (Mycobacterium tuberculosis)	73	54	708
108	11	10928	10440	gi|388109	regulatory protein (Enterococcus faecalis)	73	54	489
128	6	3632	4222	gi|1685111	orf109 (Streptococcus thermophilus)	73	63	591
138	2	1575	394	gi|147326	transport protein (Escherichia coli)	73	60	1182
140	13	12538	11903	pir|E53402|E534	serine O-acetyltransferase (EC 2.3.1.30) - Bacillus stearothermophilus	73	55	636
162	5	5701	4991	gnl|PID|e323511	putative YhaQ protein (Bacillus subtilis)	73	50	711
164	4	2323	2790	gi|1592076	hypothetical protein (SP:P25768) (Methanococcus jannaschii)	73	52	468
164	8	4815	5546	gi|410137	(ORFX1) (Bacillus subtilis)	73	56	732
170	5	4394	5302	gnl|PID|d100959	homologue of unidentified protein of E. coli (Bacillus subtilis)	73	46	909
178	7	3893	4855	gi|46242	nodulation protein B, 5'end (Rhizobium loti)	73	56	963
204	6	5096	4278	gnl|PID|e214719	PicA protein (Bacillus thuringiensis)	73	41	819
213	2	832	2037	gi|1565296	ribosomal protein S1 homolog; sequence specific DNA-binding protein (Leuconostoc lactis)	73	55	1206
231	2	84	287	gi|40173	homolog of E.coli ribosomal protein L21 (Bacillus subtilis)	73	61	204
237	1	2	505	gi|1773151	adenine phosphoribosyltransferase (Escherichia coli)	73	51	504

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
269	1	2	691	gnl|PID|d101328	YqiX (Bacillus subtilis)	73	36	690
289	2	1272	832	pir|A02771|R7HC	ribosomal protein L7/L12 - Micrococcus luteus	73	66	441
343	1	14	484	gi|1788125	(AE000276) hypothetical 30.4 kD protein in manZ-cspC intergenic region (Escherichia coli)	73	47	471
356	1	222	4	gi|2149905	D-glutamic acid adding enzyme (Enterococcus faecalis)	73	50	219
7	5	3165	4691	gnl|PID|d101833	amidase (Synechocystis sp.)	72	52	1527
7	9	7195	7647	gi|146976	nusB (Escherichia coli)	72	54	453
7	17	13743	13300	gnl|PID|e289141	similar to hydroxymyristoyl-(acyl carrier protein) dehydratase (Bacillus subtilis)	72	59	444
22	19	15637	16224	gnl|PID|d101929	ribosome releasing factor (Synechocystis sp.)	72	51	588
33	17	12111	11425	gnl|PID|d101190	ORF3 (Streptococcus mutans)	72	55	687
34	7	7147	5627	gi|396501	aspartyl-tRNA synthetase (Thermus thermophilus)	72	52	1521
38	23	15372	16085	pir|H64108|H641	L-ribulose-phosphate 4-epimerase (araD) homolog - Haemophilus influenzae (strain Rd KW20)	72	54	714
39	5	5094	6905	gnl|PID|e254877	unknown (Mycobacterium tuberculosis)	72	56	1812
40	6	4469	4636	gi|153672	lactose repressor (Streptococcus mutans)	72	58	168
48	2	1459	1253	gi|310380	inhibin beta-A-subunit (Ovis aries)	72	33	207
48	29	21729	22424	gi|2314329	(AE000623) glutamine ABC transporter, permease protein (glnP) (Helicobacter pylori)	72	49	696
50	5	4529	3288	gi|1750108	YnbA (Bacillus subtilis)	72	54	1242
51	3	1044	2282	gi|2293230	(AF008220) YtbJ (Bacillus subtilis)	72	54	1239
52	13	13681	13938	gi|142521	deoxyribodipyrimidine photolyase (Bacillus subtilis)	72	65	258
55	1	841	35	gi|882518	ORF_o304; GTG start (Escherichia coli)	72	59	807
75	5	2832	3191	gnl|PID|e209886	mercuric resistance operon regulatory protein (Bacillus subtilis)	72	44	360
76	6	6229	5771	gi|142450	ahrC protein (Bacillus subtilis)	72	53	459
79	5	5065	4592	gi|2293279	(AF008220) YtcG (Bacillus subtilis)	72	46	474
87	14	14726	12309	gnl|PID|e323502	putative PriA protein (Bacillus subtilis)	72	52	2418
91	1	464	662	gi|500691	MYO1 gene product (Saccharomyces cerevisiae)	72	50	219
91	7	4516	4764	gi|829615	skeletal muscle sodium channel alpha-subunit (Equus caballus)	72	38	249

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match accession	match gene name	% sim	% ident	length (nt)
95	2	2004	1717	gnl|PID|e323527	putative Asp23 protein (Bacillus subtilis)	72	40	288
109	1	1452	118	gi|143331	alkaline phosphatase regulatory protein (Bacillus subtilis)	72	52	1335
126	1	3	2192	gnl|PID|d101831	glutamine-binding periplasmic protein (Synechocystis sp.)	72	46	2190
130	3	1735	2478	gi|2415396	(AF015775) carboxypeptidase (Bacillus subtilis)	72	53	744
137	6	2585	2929	gi|472922	v-type Na-ATPase (Enterococcus hirae)	72	46	345
140	10	9601	9203	gi|49224	URF 4 (Synechococcus sp.)	72	48	399
146	5	1906	1247	gnl|PID|e324965	hypothetical protein (Bacillus subtilis)	72	45	660
147	2	2084	1083	gnl|PID|e325016	hypothetical protein (Bacillus subtilis)	72	56	1002
147	5	6156	5146	gi|472327	TPP-dependent acetoin dehydrogenase beta-subunit (Clostridium magnum)	72	56	1011
148	8	5381	6433	gi|974332	NAD(P)H-dependent dihydroxyacetone-phosphate reductase (Bacillus subtilis)	72	54	1053
148	14	10256	9675	gnl|PID|d101319	YqgN (Bacillus subtilis)	72	50	582
159	8	4005	4949	gi|1788770	(AE000130) o463; 24 pct identical (44 gaps) to 338 residues from penicillin-binding protein 4*, PBPE_BACSU SW: P32959 (451 aa) (Escherichia coli)	72	43	945
172	10	9907	10620	gi|763387	unknown (Saccharomyces cerevisiae)	72	55	714
220	3	2862	3602	gi|1574175	hypothetical (Haemophilus influenzae)	72	50	741
267	1	3	449	gi|290513	f470 (Escherichia coli)	72	48	447
281	2	899	540	gnl|PID|d100964	homologue of aspartokinase 2 alpha and beta subunits LysC of B. subtilis (Bacillus subtilis)	72	45	360
290	1	1018	14	gi|474195	This ORF is homologous to a 40.0 kd hypothetical protein in the htrB 3' region from E. coli, Accession Number X61000 (Mycoplasma-like organism)	72	54	1005
300	1	63	587	gi|746399	transcription elongation factor (Escherichia coli)	72	50	525
316	1	1326	4	gi|158127	protein kinase C (Drosophila melanogaster)	72	40	1323
342	1	227	3	gnl|PID|d101164	unknown (Bacillus subtilis)	72	54	225
354	1	1	1005	gnl|PID|d102048	C. thermocellum beta-glucosidase; P26208 (985) (Bacillus subtilis)	72	52	1005
6	10	8134	10467	gnl|PID|e264229	unknown (Mycobacterium tuberculosis)	71	57	2334
7	20	16231	15464	gi|18046	3-oxoacyl-(acyl-carrier protein) reductase (Cuphea lanceolata)	71	52	768
15	1	1297	2	gnl|PID|d100571	replicative DNA helicase (Bacillus subtilis)	71	51	1296
15	4	4435	3869	gi|499384	orf189 (Bacillus subtilis)	71	47	567

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
18	6	5120	4218	gnl|PID|d101318	YqgG (Bacillus subtilis)	71	51	903
29	1	1	540	gi|1773142	similar to the 20.2kd protein in TETB-EXOA region of B. subtilis (Escherichia coli)	71	56	540
38	20	13327	13830	gi|537036	ORF_o158 (Escherichia coli)	71	48	504
51	12	15015	12676	gi|149528	dipeptidyl peptidase IV (Lactococcus lactis)	71	55	2340
5.	23	21040	20585	gi|2343285	(AF015453) surface located protein (Lactobacillus rhamnosus)	71	58	456
60	2	705	265	gnl|PID|d101320	YqgZ (Bacillus subtilis)	71	44	441
71	18	24679	26226	gi|580920	rodD (gtaA) polypeptide (AA 1-673) (Bacillus subtilis)	71	44	1548
71	25	30587	30360	gi|606028	ORF_o414; Geneplot suggests frameshift near start but none found (Escherichia coli)	71	50	228
72	6	5219	6729	gi|580835	lysine decarboxylase (Bacillus subtilis)	71	48	1491
72	14	11991	12878	gi|624085	similar to rat beta-alanine synthetase encoded by GenBank Accession Number S27881; contains ATP/GTP binding motif (Paramecium bursaria Chlorella virus 1)	71	54	888
73	11	7269	7033	gi|1906594	PNI (Rattus norvegicus)'			
74	6	10385	8517	gi|1573733	prolyl-tRNA synthetase (proS) (Haemophilus influenzae)	71	42	237
81	9	5772	6578	gi|147404	mannose permease subunit II-H-Man (Escherichia coli)	71	52	1869
86	5	4602	3604	gnl|PID|e322063	ss-1,4-galactosyltransferase (Streptococcus pneumoniae)	71	45	807
105	4	3619	4707	gi|2323341	(AF014460) PepQ (Streptococcus mutans)	71	53	999
106	13	13557	12955	gi|1519287	LemA (Listeria monocytogenes)	71	58	1089
114	2	1029	1979	gi|310303	mosA (Rhizobium meliloti)	71	48	603
122	2	564	1205	gi|1649037	glutamine transport ATP-binding protein GLNQ (Salmonella typhimurium)	71	55	951
132	5	9018	7063	gnl|PID|d102049	H. influenzae hypothetical ABC transporter; P44808 (974) (Bacillus subtilis)	71	50	642
140	1	1141	227	gi|1673788	(AE000015) Mycoplasma pneumoniae, fructose-bisphosphate aldolase; similar to Swiss-Prot Accession Number P13243, from B subtilis (Mycoplasma pneumoniae)	71	51	1956
140	5	5635	4973	gnl|PID|d100964	homologue of hypothetical protein in a rapamycin synthesis gene cluster of Streptomyces hygroscopicus (Bacillus subtilis)	71	49	915
141	7	7369	7845	gnl|PID|d102005	(AB001488) FUNCTION UNKNOWN, SIMILAR PRODUCT IN E. COLI AND MYCOPLASMA PNEUMONIAE. (Bacillus subtilis)	71	48	663
						71	51	477

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
193	1	1	165	gi|46912	ribosomal protein L13 (Staphylococcus carnosus)	71	59	165
194	3	2205	1594	gi|535351	CodY (Bacillus subtilis)	71	52	612
199	3	1510	1319	gi|2182574	(AE000090) Y4pE (Rhizobium sp. NGR234)	71	45	192
208	2	2616	3752	gi|1787378	(AE000213) hypothetical protein in purB 5' region (Escherichia coli)	71	57	1137
209	2	2022	1141	gi|41432	fepC gene product (Escherichia coli)	71	46	882
210	5	1911	3071	gi|49316	ORF2 gene product (Bacillus subtilis)	71	45	1161
210	6	3069	3386	gi|580900	ORF3 gene product (Bacillus subtilis)	71	48	318
212	2	3561	1381	gi|557567	ribonucleotide reductase R1 subunit (Mycobacterium tuberculosis)	71	53	2181
233	3	2003	2920	gnl|PID|d101320	YqgR (Bacillus subtilis)	71	50	918
244	1	13	1053	gnl|PID|d100964	homologue of aspartokinase 2 alpha and beta subunits LysC of B. subtilis (Bacillus subtilis)	71	55	1041
251	2	1008	1874	gi|755601	unknown (Bacillus subtilis)	71	46	867
282	2	906	712	gi|1353874	unknown (Rhodobacter capsulatus)	71	46	195
312	4	2137	1565	gnl|PID|d102245	(AB005556) yxbF (Bacillus subtilis)	71	34	573
338	1	3	683	gi|1591045	hypothetical protein (SP:P31466) (Methanococcus jannaschii)	71	48	681
346	1	3	164	gi|1591234	hypothetical protein (SP:P42297) (Methanococcus jannaschii)	71	36	162
374	1	619	2	gi|397526	clumping factor (Staphylococcus aureus)	71	23	618
377	1	688	2	gi|397526	clumping factor (Staphylococcus aureus)	71	23	687
3	8	7419	6958	gnl|PID|e269486	Unknown (Bacillus subtilis)	70	42	462
3	10	8395	9075	gnl|PID|e255543	putative iron dependant repressor (Staphylococcus epidermidis)	70	46	681
7	16	11024	10254	gnl|PID|d100290	undefined open reading frame (Bacillus stearothermophilus)	70	55	771
7	18	14213	13719	gnl|PID|d101090	biotin carboxyl carrier protein of acetyl-CoA carboxylase (Synechocystis sp.)	70	56	495
9	2	1057	287	gnl|PID|d100581	unknown (Bacillus subtilis)	70	52	771
12	4	2610	1789	gnl|PID|d101195	yycJ (Bacillus subtilis)	70	52	822
21	2	2586	1846	gi|2293447	(AF008930) ATPase (Bacillus subtilis)	70	54	741
22	13	10955	11512	gi|1165295	Ydr540cp (Saccharomyces cerevisiae)	70	50	558
30	6	4315	3980	gi|39478	ATP binding protein of transport ATPases (Bacillus firmus)	70	51	336

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
31	1	370	113	gi|662792	single-stranded DNA binding protein (unidentified eubacterium)	70	36	258
33	15	10639	9521	gi|1161219	homolgous to D-amino acid dehydrogenase enzyme (Pseudomonas aeruginosa)	70	50	1119
38	6	3812	4312	gi|2058547	ComYD (Streptococcus gordonii)	70	48	501
38	25	17986	18477	gi|537033	ORF_f356 (Escherichia coli)	70	58	492
40	13	11054	9846	gi|1173516	riboflavin-specific deaminase (Actinobacillus pleuropneumoniae)	70	52	1209
42	2	722	1954	gi|1146183	putative (Bacillus subtilis)	70	51	1233
43	3	2373	1612	gi|1591493	glutamine transport ATP-binding protein Q (Methanococcus jannaschii)	70	48	762
45	8	9197	8049	gnl|PID|d102036	subunit of ADP-glucose pyrophosphorylase (Bacillus stearothermophilus)	70	54	1149
59	2	567	956	gnl|PID|d100302	neopullulanase (Bacillus sp.)	70	42	390
60	3	1874	795	gnl|PID|e276466	aminopeptidase P (Lactococcus lactis)	70	48	1080
61	4	5553	2437	gnl|PID|e275074	SNF (Bacillus cereus)	70	51	3117
61	7	7914	6802	gi|1573037	cystathionine gamma-synthase (metB) (Haemophilus influenzae)	70	52	1113
63	7	5372	7222	gnl|PID|d100974	unknown (Bacillus subtilis)	70	54	1851
68	7	7126	6962	gi|1263014	emm18.1 gene product (Streptococcus pyogenes)	70	37	165
72	12	10081	10911	gi|2313093	(AE000524) carboxynorspermidine decarboxylase (nspC) (Helicobacter pylori)	70	56	831
75	10	7888	8124	gi|1077423	galactose-1-P-uridyl transferase (Streptococcus mutans)	70	59	237
79	3	3424	2525	gi|39881	ORF 311 (AA 1-311) (Bacillus subtilis)	70	47	900
87	10	9369	7324	gnl|PID|e323506	putative Pkn2 protein (Bacillus subtilis)	70	52	2046
96	14	10640	11788	gi|1573209	tRNA-guanine transglycosylase (tgt) (Haemophilus influenzae)	70	52	1149
113	2	574	1086	gi|433630	A180 (Saccharomyces cerevisiae)	70	59	513
123	5	2901	3461	gnl|PID|d100585	unknown (Bacillus subtilis)	70	45	561
125	5	4593	4282	gnl|PID|e276474	capacitative calcium entry channel 1 (Bos taurus)	70	35	312
129	5	4500	3454	gnl|PID|d101314	YqeT (Bacillus subtilis)	70	47	1047
133	3	2608	1394	gi|2293312	(AF008220) YtfP (Bacillus subtilis)	70	50	1215
135	1	420	662	gnl|PID|e265530	yorfE (Streptococcus pneumoniae)	70	47	243
137	3	438	932	gi|472919	v-type Na-ATPase (Enterococcus hirae)	70	57	495
138	1	440	3	gi|147336	transmembrane protein (Escherichia coli)	70	42	438

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
31	1	370	111	gi|662792	single-stranded DNA binding protein (unidentified eubacterium)	70	36	258
33	15	10639	9521	gi|1161219	homolgous to D-amino acid dehydrogenase enzyme (Pseudomonas aeruginosa)	70	50	1119
38	6	3812	4312	gi|2058547	ComYD (Streptococcus gordonii)	70	48	501
38	25	17986	18477	gi|537033	ORF_f356 (Escherichia coli)	70	58	492
40	13	11054	9846	gi|1173516	riboflavin-specific deaminase (Actinobacillus pleuropneumoniae)	70	52	1209
42	2	722	1954	gi|1146183	putative (Bacillus subtilis)	70	51	1233
43	3	2373	1612	gi|1591493	glutamine transport ATP-binding protein Q (Methanococcus jannaschii)	70	48	762
45	8	9197	8049	gnl|PID|d102036	subunit of ADP-glucose pyrophosphorylase (Bacillus stearothermophilus)	70	54	1149
59	2	567	956	gnl|PID|d100302	neopullulanase (Bacillus sp.)	70	42	390
60	3	1874	795	gnl|PID|e276466	aminopeptidase P (Lactococcus lactis)	70	48	1080
61	4	5553	2437	gnl|PID|e275074	SNF (Bacillus cereus)	70	51	3117
61	7	7914	6802	gi|1573037	cystathionine gamma-synthase (metB) (Haemophilus influenzae)	70	52	1113
63	7	5372	7222	gnl|PID|d100974	unknown (Bacillus subtilis)	70	54	1851
68	7	7126	6962	gi|1263014	emm18.1 gene product (Streptococcus pyogenes)	70	37	165
72	12	10081	10911	gi|2313093	(AE000524) carboxynorspermidine decarboxylase (nspC) (Helicobacter pylori)	70	56	831
75	10	7888	8124	gi|1877423	galactose-1-P-uridyl transferase (Streptococcus mutans)	70	59	237
79	3	3424	2525	gi|39881	ORF 311 (AA 1-311) (Bacillus subtilis)	70	47	900
87	10	9369	7324	gnl|PID|e323506	putative Pkn2 protein (Bacillus subtilis)	70	52	2046
96	14	10640	11788	gi|1573209	tRNA-guanine transglycosylase (tgt) (Haemophilus influenzae)	70	52	1149
113	2	574	1086	gi|433630	A180 (Saccharomyces cerevisiae)	70	59	513
123	5	2901	3461	gnl|PID|d100585	unknown (Bacillus subtilis)	70	45	561
125	5	4593	4282	gnl|PID|e276474	capacitative calcium entry channel 1 (Bos taurus)	70	35	312
129	5	4500	3454	gnl|PID|d101314	YqeT (Bacillus subtilis)	70	47	1047
133	3	2608	1394	gi|2293312	(AF008220) YtfP (Bacillus subtilis)	70	50	1215
135	1	420	662	gnl|PID|e265530	yorfE (Streptococcus pneumoniae)	70	47	243
137	3	438	932	gi|472919	v-type Na-ATPase (Enterococcus hirae)	70	57	495
138	1	440	3	gi|147336	transmembrane protein (Escherichia coli)	70	42	438

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match accession	match gene name	% sim	% ident	length (nt)
140	16	18796	16364	gi|976441	N5-methyltetrahydrofolate homocysteine methyltransferase (Saccharomyces cerevisiae)	70	53	2433
167	10	8263	6695	gi|149535	D-alanine activating enzyme (Lactobacillus casei)	70	52	1569
204	4	3226	2747	gnl|PID|d102049	E. coli hypothetical protein; P31805 (267) (Bacillus subtilis)	70	51	480
207	3	2627	2869	gnl|PID|e309213	racGAP (Dictyostelium discoideum)	70	45	243
282	3	1136	882	gi|1353874	unknown (Rhodobacter capsulatus)	70	50	255
6	21	17554	18453	gnl|PID|e233879	hypothetical protein (Bacillus subtilis)	69	44	900
6	22	18482	19471	gi|580883	ipa-88d gene product (Bacillus subtilis)	69	53	990
22	6	4682	5824	gi|2209379	(AF006720) ProJ (Bacillus subtilis)	69	48	1143
22	9	7992	8651	gnl|PID|d100580	unknown (Bacillus subtilis)	69	51	660
22	12	9871	10767	gnl|PID|d100581	unknown (Bacillus subtilis)	69	51	897
27	7	5857	5348	gnl|PID|d102012	(AB001488) FUNCTION UNKNOWN. (Bacillus subtilis)	69	28	510
36	10	7294	10116	gi|437916	isoleucyl-tRNA synthetase (Staphylococcus aureus)	69	53	2823
38	1	2	1090	gi|141900	alcohol dehydrogenase (EC 1.1.1.1) (Alcaligenes eutrophus)	69	48	1089
40	14	11333	11944	gi|1573280	Holliday junction DNA helicase (ruvA) (Haemophilus influenzae)	69	44	612
40	15	11942	12517	gi|1573653	DNA-3-methyladenine glycosidase I (tagI) (Haemophilus influenzae)	69	50	576
45	6	6947	5490	gi|580887	starch (bacterial glycogen) synthase (Bacillus subtilis)	69	47	1458
48	34	24932	24153	gnl|PID|e233870	hypothetical protein (Bacillus subtilis)	69	36	780
49	6	6183	6521	gi|396297	similar to phosphotransferase system enzyme II (Escherichia coli)	69	50	339
49	8	7586	8338	gi|396420	similar to Alcaligenes eutrophus pHG1 D-ribulose-5-phosphate 3 epimerase (Escherichia coli)	69	49	753
55	6	8262	7033	gi|1146238	poly(A) polymerase (Bacillus subtilis)	69	50	1230
59	3	954	2333	gnl|PID|e313038	hypothetical protein (Bacillus subtilis)	69	54	1380
62	3	1170	1418	gnl|PID|d101915	hypothetical protein (Synechocystis sp.)	69	49	249
63	8	7298	7762	gi|293017	ORF3 (put.); putative (Lactococcus lactis)	69	42	465
66	4	3657	5081	gi|153755	phospho-beta-D-galactosidase (EC 3.2.1.85) (Lactococcus lactis cremoris)	69	49	1425
66	5	5126	6829	gi|433809	enzyme II (Streptococcus mutans)	69	46	1704
71	6	10017	10664	gnl|PID|e322063	ss-1,4-galactosyltransferase (Streptococcus pneumoniae)	69	39	648

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
71	21	27730	27966	gnl|PID|d100649	DE-cadherin (Drosophila melanogaster)	69	30	237
77	1	1	237	gi|287870	groES gene product (Lactococcus lactis)	69	44	237
81	5	3622	4101	gi|1573605	fucose operon protein (fucU) (Haemophilus influenzae)	69	52	480
83	1	40	714	pir|C33496|C334	hisC homolog - Bacillus subtilis	69	46	675
83	16	15742	16335	gi|143372	phosphoribosyl glycinamide formyltransferase (PUR-N) (Bacillus subtilis)	69	46	594
85	2	1212	916	gi|194097	IFN-response element binding factor 1 (Mus musculus)	69	48	297
91	5	3678	4274	gi|1574712	anaerobic ribonucleoside-triphosphate reductase activating protein (nrdG) (Haemophilus influenzae)	69	44	597
98	5	3247	4032	gnl|PID|d100262	LivF protein (Salmonella typhimurium)	69	51	786
108	5	4085	5056	gnl|PID|e257629	transcription factor (Lactococcus lactis)	69	49	972
126	3	3078	4568	gnl|PID|d101329	YqjJ (Bacillus subtilis)	69	49	1491
131	6	4121	2889	gnl|PID|d101314	YqeR (Bacillus subtilis)	69	47	1233
136	2	1505	2299	gnl|PID|d100581	unknown (Bacillus subtilis)	69	47	795
149	5	3852	4763	gnl|PID|e233525	YloQ protein (Bacillus subtilis)	69	50	912
149	12	9336	10655	gi|151571	Homology with E.coli and P.aeruginosa lysA gene; product of unknown function; putative (Pseudomonas syringae)	69	52	1320
153	4	3191	3829	gi|1710373	BrnQ (Bacillus subtilis)	69	44	639
169	3	849	2324	gnl|PID|d100582	temperature sensitive cell division (Bacillus subtilis)	69	49	1476
180	1	566	3	gi|488339	alpha-amylase (unidentified cloning vector)	69	50	564
212	1	1196	231	gi|1395209	ribonucleotide reductase R2-2 small subunit (Mycobacterium tuberculosis)	69	53	966
226	1	2	661	pir|JQ2285|JQ22	nodulin-26 - soybean	69	41	660
233	5	3249	4766	gi|472918	v-type Na-ATPase (Enterococcus hirae)	69	56	1518
235	3	660	1766	gi|148945	methylase (Haemophilus influenzae)	69	43	1107
243	2	865	2361	gnl|PID|d100225	ORF5 (Barley yellow dwarf virus)	69	69	1497
251	3	2899	1967	gi|2289231	macrolide-efflux protein (Streptococcus agalactiae)	69	51	933
310	1	1	282	gnl|PID|e322442	peptide deformylase (Clostridium beijerinckii)	69	55	282
369	1	868	2	gi|397526	clumping factor (Staphylococcus aureus)	69	22	867
370	1	749	3	gi|397526	clumping factor (Staphylococcus aureus)	69	21	747

TABLE 2

S pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match accession	match gene name	% sim	% ident	length (nt)
379	1	44	280	gnl|PID|d100649	DE-cadherin (Drosophila melanogaster)	69	30	237
388	1	260	72	gi|1787524	(AE000225) hypothetical 32.7 kD protein in trpL-btuR intergenic region (Escherichia coli)	69	44	189
1	2	2006	3040	gnl|PID|d101809	ABC transporter (Synechocystis sp.)	68	43	1035
12	5	3958	2600	gi|2182992	histidine kinase (Lactococcus lactis cremoris)	68	45	1359
15	2	1790	1311	pir|S16974|R5BS	ribosomal protein L9 - Bacillus stearothermophilus	68	56	480
16	6	7353	5701	gi|1787041	(AE000184) o530; This 530 aa orf is 33 pct identical (14 gaps) to 525 residues of an approx. 640 aa protein YHES_HAEIN SW: P44808 (Escherichia coli)	68	45	1653
17	12	6479	6805	gi|553165	acetylcholinesterase (Homo sapiens)	68	68	327
20	13	14128	14505	gi|142700	P competence protein (ttg start codon) (put.); putative (Bacillus subtilis)	68	40	378
22	32	24612	25397	gi|289262	comE ORF) (Bacillus subtilis)	68	36	786
30	7	4548	4288	gi|311388	ORF1 (Azorhizobium caulinodans)	68	46	261
36	5	3911	4585	gi|1573041	hypothetical (Haemophilus influenzae)	68	54	675
46	6	5219	6040	gi|1790131	(AE000446) hypothetical 29.7 kD protein in ibpA-gyrB intergenic region (Escherichia coli)	68	47	822
54	10	6235	7086	gi|882579	CG Site No. 29739 (Escherichia coli)	68	55	852
55	5	7069	5165	gnl|PID|d101914	ABC transporter (Synechocystis sp.)	68	45	1905
71	3	6134	5613	gi|1573353	outer membrane integrity protein (tolA) (Haemophilus influenzae)	68	50	522
71	10	15342	16613	gi|580866	ipa-12d gene product (Bacillus subtilis)	68	31	1272
71	12	17560	18792	gi|44073	SecY protein (Lactococcus lactis)	68	35	1233
71	17	22295	24703	gi|1762349	involved in protein export (Bacillus subtilis)	68	50	2409
73	16	10208	9729	gi|1353537	dUTPase (Bacteriophage rit)	68	51	480
86	18	17198	16011	gi|413943	ipa-19d gene product (Bacillus subtilis)	68	53	1188
87	17	17491	15866	gi|150209	ORF 1 (Mycoplasma mycoides)	68	43	1626
89	6	5139	4354	gi|1498824	M. jannaschii predicted coding region MJ0062 (Methanococcus jannaschii)	68	40	786
89	11	8021	8242	gi|150974	4-oxalocrotonate tautomerase (Pseudomonas putida)	68	43	222
97	8	6755	5394	gi|2367358	(AE000491) hypothetical 52.9 kD protein in aldB-rpsF intergenic region (Escherichia coli)	68	41	1362

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
98	3	1418	2308	gnl|PID|d100261	LivA protein (Salmonella typhimurium)	68	40	891
99	13	16414	17280	gi|455363	regulatory protein (Streptococcus mutans)	68	50	867
115	3	5054	3693	gi|466474	cellobiose phosphotransferase enzyme II'' (Bacillus stearothermophilus)	68	44	1362
124	7	3394	3221	gnl|PID|d100702	cut14 protein (Schizosaccharomyces pombe)	68	56	174
125	2	2923	1922	gi|450566	transmembrane protein (Bacillus subtilis)	68	50	1002
132	2	4858	2888	gnl|PID|d101732	DNA ligase (Synechocystis sp.)	68	52	1971
140	7	7765	7580	gi|1209711	unknown (Saccharomyces cerevisiae)	68	47	186
150	1	539	3	gi|402490	ADP-ribosylarginine hydrolase (Mus musculus)	68	59	537
164	1	58	867	gnl|PID|e255114	glutamate racemase (Bacillus subtilis)	68	49	810
	2	819	1835	gnl|PID|e255117	hypothetical protein (Bacillus subtilis)	68	50	1017
169	7	3946	4104	pir|B54545|B545	hypothetical protein - Lactococcus lactis subsp. lactis plasmid pSL2	68	40	159
170	4	4247	4396	gi|304146	spore coat protein (Bacillus subtilis)	68	52	150
171	8	6002	7054	gi|38722	precursor (aa -20 to 381) (Acinetobacter calcoaceticus)	68	54	1053
198	3	2473	1871	gnl|PID|e313075	hypothetical protein (Bacillus subtilis)	68	46	603
211	2	969	1802	gi|1439528	EIIC-man (Lactobacillus curvatus)	68	45	834
214	8	4926	4231	gnl|PID|d102049	H. influenzae hypothetical protein; P43990 (182) (Bacillus subtilis)	68	50	696
217	6	4955	5170	gnl|PID|e326966	similar to B.vulgaris CMS-associated mitochondrial ... (reverse transcriptase) (Arabidopsis thaliana)	68	36	216
218	7	3930	4745	gi|2293198	(AF008220) YtgP (Bacillus subtilis)	68	38	816
220	6	4628	4338	gnl|PID|e325791	(AJ000005) orf1 (Bacillus megaterium)	68	51	291
236	1	746	108	gi|410137	ORFX13 (Bacillus subtilis)	68	46	639
237	2	675	1451	gi|396348	homoserine transsuccinylase (Escherichia coli)	68	49	777
250	4	771	1229	gi|310859	ORF2 (Synechococcus sp.)	68	50	459
254	1	517	155	gi|1787105	(AE000189) o648 was o669; This 669 aa orf is 40 pct identical (1 gaps) to 217 residues of an approx. 232 aa protein YBBA_HAEIN SW: P45247 (Escherichia coli)	68	44	363
337	1	1	774	gnl|PID|e261990	putative orf (Bacillus subtilis)	68	47	774
345	1	3	653	gi|149513	thymidylate synthase (EC 2.1.1.45) (Lactococcus lactis)	68	61	651

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
386	2	417	4	gi|1573353	outer membrane integrity protein (tolA) (Haemophilus influenzae)	68	51	414
2	4	5722	4697	gi|1592141	H. jannaschii predicted coding region MJ1507 (Methanococcus jannaschii)	67	26	1026
3	6	5397	4591	gi|2293175	(AF008220) signal transduction regulator (Bacillus subtilis)	67	44	807
5	2	2301	574	gi|2313385	(AE000547) para-aminobenzoate synthetase (pabB) (Helicobacter pylori)	67	48	1728
6	19	16063	16758	gi|413931	ipa-7d gene product (Bacillus subtilis)	67	41	696
22	8	7094	7897	gi|1928962	pyrroline-5-carboxylate reductase (Actinidia deliciosa)	67	51	804
29	10	8335	9072	gi|468745	gtcR gene product (Bacillus brevis)	67	41	738
31	3	1379	585	gi|2425123	(AF019986) PksB (Dictyostelium discoideum)	67	49	795
32	11	8849	10150	gi|42029	ORF1 gene product (Escherichia coli)	67	47	1302
36	16	14830	15546	gi|1592142	ABC transporter, probable ATP-binding subunit (Methanococcus jannaschii)	67	43	717
38	9	4958	5392	gnl|PID|e214803	T22B3.3 (Caenorhabditis elegans)	67	47	435
38	21	13775	14512	gi|537037	ORF_o216 (Escherichia coli)	67	52	738
45	9	10428	9181	gi|551710	branching enzyme (glgB) (EC 2.4.1.18) (Bacillus stearothermophilus)	67	51	1248
48	23	18344	17514	gi|413949	ipa-25d gene product (Bacillus subtilis)	67	50	831
50	2	1773	952	gnl|PID|d101330	YqjQ (Bacillus subtilis)	67	55	822
53	1	431	3	gi|1574291	fimbrial transcription regulation repressor (pilB) (Haemophilus influenzae)	67	40	429
55	13	12740	11946	gnl|PID|e252990	ORF YDL037c (Saccharomyces cerevisiae)	67	51	795
61	9	9210	8329	gnl|PID|e264711	ATP-binding cassette transporter A (Staphylococcus aureus)	67	50	882
71	2	5614	6117	gi|1197667	vitellogenin (Anolis pulchellus)	67	36	504
81	7	4489	4983	gi|1142714	phosphoenolpyruvate:mannose phosphotransferase element IIB (Lactobacillus curvatus)	67	42	495
83	7	2957	3214	gi|1276746	Acyl carrier protein (Porphyra purpurea)	67	37	258
86	8	8140	6809	gi|1147744	PSR (Enterococcus hirae)	67	45	1332
97	3	986	1366	gnl|PID|d102235	(AB000631) unnamed protein product (Streptococcus mutans)	67	43	381
102	1	601	1413	gi|682765	mccB gene product (Escherichia coli)	67	36	813
106	3	1109	1987	gi|148921	LicD protein (Haemophilus influenzae)	67	43	879
115	4	5982	5656	gi|895750	putative cellobiose phosphotransferase enzyme III (Bacillus subtilis)	67	44	327

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
115	7	8421	8077	gi|466473	cellobiose phosphotransferase enzyme II' (Bacillus stearothermophilus)	67	51	345
127	13	8127	7021	gi|147326	transport protein (Escherichia coli)	67	45	1107
136	3	2215	2859	gnl|PID|d100581	unknown (Bacillus subtilis)	67	49	645
140	21	23317	20906	gnl|PID|d101912	phenylalanyl-tRNA synthetase (Synechocystis sp.)	67	43	2412
146	6	2894	1893	gi|2182994	histidine kinase (Lactococcus lactis cremoris)	67	44	1002
151	8	11476	11117	gnl|PID|d100085	ORF129 (Bacillus cereus)	67	48	360
160	10	7453	8646	gi|2281317	OrfB; similar to a Streptococcus pneumoniae putative membrane protein encoded by GenBank Accession Number X99400; inactivation of the OrfB gene leads to UV-sensitivity and to decrease of homologous recombination (plasmidic test) (Lactococcus l	67	46	1194
161	3	3099	4505	gnl|PID|d101317	YqfA (Bacillus subtilis)	67	47	1407
167	8	6704	5454	gi|1161933	DltB (Lactobacillus casei)	67	45	1251
169	4	2322	2879	gnl|PID|d101331	YqkG (Bacillus subtilis)	67	41	558
171	11	7656	8384	gi|153841	pneumococcal surface protein A (Streptococcus pneumoniae)	67	50	729
188	3	1930	3723	gi|1542975	AbcB (Thermoanaerobacterium thermosulfurigenes)	67	46	1794
189	6	3599	3141	gnl|PID|e325178	Hypothetical protein (Bacillus subtilis)	67	52	459
205	3	1663	2211	gi|606073	ORF_o169 (Escherichia coli)	67	47	549
207	4	2896	3456	gi|2276174	DtxR/iron regulated lipoprotein precursor (Corynebacterium diphtheriae)	67	49	561
217	3	4086	3703	gi|895750	putative cellobiose phosphotransferase enzyme III (Bacillus subtilis)	67	42	384
246	2	291	662	gi|1842438	unknown (Bacillus subtilis)	67	43	372
252	1	2	745	gi|2351768	PspA (Streptococcus pneumoniae)	67	41	744
265	3	1134	1811	gi|2313847	(AE000585) L-asparaginase II (ansB) (Helicobacter pylori)	67	42	678
295	1	1	375	gi|2276174	DtxR/iron regulated lipoprotein precursor (Corynebacterium diphtheriae)	67	43	375
1	7	4898	5146	gnl|PID|e255179	unknown (Mycobacterium tuberculosis)	66	56	249
3	1	389	3	gnl|PID|e269548	Unknown (Bacillus subtilis)	66	48	387
3	20	19267	20805	gi|39956	IIGlc (Bacillus subtilis)	66	50	1539
4	3	2545	2718	gi|1787564	(AE000228) phage shock protein C (Escherichia coli)	66	36	174
5	9	13197	12592	gi|1574291	fimbrial transcription regulation repressor (pilB) (Haemophilus influenzae)	66	46	606

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
9	4	2872	1451	|gnl|PID|e266928	|unknown (Mycobacterium tuberculosis)	66	43	1422
12	2	1469	1200	|gi|520407	|orf2; GTG start codon (Bacillus thuringiensis)	66	42	270
15	12	10979	9897	|gi|2314738	|(AE000653) translation elongation factor EF-Ts (tsf) (Helicobacter pylori)	66	49	1083
16	2	1312	734	|gnl|PID|d102245	|(AB005554) yxbF (Bacillus subtilis)	66	35	579
22	3	1372	1851	|gi|1480916	|signal peptidase type II (Lactococcus lactis)	66	38	480
22	7	5828	7096	|gnl|PID|e206261	|gamma-glutamyl phosphate reductase (Streptococcus thermophilus)	66	51	1269
22	20	16194	17138	|gnl|PID|e281914	|YitL (Bacillus subtilis)	66	50	945
30	2	530	976	|gi|2314379	|(AE000627) ABC transporter, ATP-binding protein (yhcG) (Helicobacter pylori)	66	40	447
32	1	199	984	|gi|312444	|ORF2 (Bacillus caldolyticus)	66	49	786
33	13	8352	7234	|gi|1387979	|44% identity over 302 residues with hypothetical protein from Synechocystis sp. accession D64006_CD; expression induced by environmental stress; some similarity to glycosyl transferases; two potential membrane-spanning helices (Bacillus subtil	66	44	1119
34	6	5658	4708	|gnl|PID|e250724	|orf2 (Lactobacillus sake)	66	39	951
34	14	9792	9574	|gi|1590997	|M. jannaschii predicted coding region MJ0272 (Methanococcus jannaschii)	66	48	219
35	16	15163	14501	|gi|1773352	|CapSM (Staphylococcus aureus)	66	46	663
36	9	6173	6976	|gi|1518680	|minicell-associated protein DivIVA (Bacillus subtilis)	66	35	804
36	11	10396	10824	|bbs|155344	|insulin activator factor, INSAF (human, Pancreatic insulinoma, Peptide Partial, 744 aa) (Homo sapiens)	66	43	429
48	1	28	1419	|gnl|PID|e325204	|hypothetical protein (Bacillus subtilis)	66	50	1392
48	7	3810	4112	|gi|2102574	|(AE000090) YdpE (Rhizobium sp. NGR234)	66	40	303
52	4	3595	2789	|gi|388565	|major cell-binding factor (Campylobacter jejuni)	66	52	807
54	3	2662	1076	|gnl|PID|d101831	|glutamine-binding periplasmic protein (Synechocystis sp.)	66	43	1587
61	10	9740	9183	|gnl|PID|e154144	|mdr gene product (Staphylococcus aureus)	66	44	558
72	13	10893	11993	|gi|2313129	|(AE000526) H. pylori predicted coding region HP0049 (Helicobacter pylori)	66	44	1101
74	9	13267	12476	|gi|1573941	|hypothetical (Haemophilus influenzae)	66	43	792
75	1	2	868	|gi|1574631	|nicotinamide mononucleotide transporter (pnuC) (Haemophilus influenzae)	66	48	867
75	7	5303	4275	|gi|41312	|put. EBG repressor protein (Escherichia coli)	66	40	1029

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
82	7	6813	8123	gnl|PID|e255128	trigger factor (Bacillus subtilis)	66	53	1311
83	3	905	1219	pir|C33496|C33496	hisC homolog - Bacillus subtilis	66	44	315
86	10	9407	8925	gi|603584	shikimate kinase (Lactococcus lactis)	66	41	483
88	10	7001	6060	gi|2098719	putative fimbrial-associated protein (Actinomyces naeslundii)	66	52	942
89	1	951	4	gi|410118	ORFX19 (Bacillus subtilis)	66	41	948
93	7	3661	2711	gi|1787936	(AE000260) f298; This 298 aa orf is 51 pct identical (5 gaps) to 297 residues of an approx. 304 aa protein YCSH_BACSU SW: P42972 (Escherichia coli)	66	49	951
104	3	1805	3049	gi|1469784	putative cell division protein ftsW (Enterococcus hirae)	66	48	1245
106	14	13576	14253	gi|40027	homologous to E.coli gldB (Bacillus subtilis)	66	52	678
107	3	965	1864	gi|144858	ORF A (Clostridium perfringens)	66	49	900
112	7	5718	6593	gi|609332	DprA (Haemophilus influenzae)	66	43	876
115	1	3	302	gi|727367	Hyr1p (Saccharomyces cerevisiae)	66	56	300
122	1	3.	566	gnl|PID|d101328	YqiY (Bacillus subtilis)	66	36	564
126	8	11759	11046	gnl|PID|d101163	ORF3 (Bacillus subtilis)	66	48	714
128	11	8201	8431	gi|726288	growth associated protein GAP-43 (Xenopus laevis)	66	41	231
131	8	4894	4508	gi|486661	TMna related protein (Saccharomyces cerevisiae)	66	39	387
140	3	3236	2574	gi|40056	phoP gene product (Bacillus subtilis)	66	36	663
140	15	16318	15434	gi|1658189	5,10-methylenetetrahydrofolate reductase (Erwinia carotovora)	66	48	885
146	12	7926	7636	gnl|PID|d101140	transposase (Synechocystis sp.)	66	42	291
147	6	7137	6154	gi|472326	TPP-dependent acetoin dehydrogenase alpha-subunit (Clostridium magnum)	66	48	984
149	6	4435	5430	gnl|PID|d101887	pentose-5-phosphate-3-epimerase (Synechocystis sp.)	66	46	996
149	13	10754	11575	gi|42371	pyruvate formate-lyase activating enzyme (AA 1-246) (Escherichia coli)	66	42	822
186	4	2578	2270	gnl|PID|d101199	ORF11 (Enterococcus faecalis)	66	41	309
207	2	2340	2597	gnl|PID|e321893	envelope glycoprotein gp160 (Human immunodeficiency virus type 1)	66	46	258
210	7	3358	3678	gi|49318	ORF4 gene product (Bacillus subtilis)	66	46	321
217	8	5143	5355	gi|49538	thrombin receptor (Cricetulus longicaudatus)	66	38	213
220	4	3875	3642	gi|466648	alternate name ORFD of L23635 (Escherichia coli)	66	33	234

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
223	1	1070	138	|gnl|PID|e247187	|zinc finger protein |Bacteriophage phig1e|	66	45	933
224	2	1864	2640	|gi|1176199	|putative ABC transporter subunit |Staphylococcus epidermidis|	66	41	777
243	1	3	872	|dbj||AB000617_2	|(AB000617) YcdH |Bacillus subtilis|	66	45	870
268	2	891	568	|gi|517210	|putative transposase |Streptococcus pyogenes|	66	60	324
322	1	2	643	|gi|1499836	|Zn protease |Methanococcus jannaschii|	66	40	642
5	10	13909	13178	|gi|1574292	|hypothetical |Haemophilus influenzae|	65	34	732
6	11	10465	11190	|gi|142854	|homologous to E. coli radC gene product and to unidentified protein from Staphylococcus aureus |Bacillus subtilis|	65	48	726
7	2	647	405	|pir|C64146|C641	|hypothetical protein HI0259 - Haemophilus influenzae (strain Rd KW20)	65	42	243
7	7	6246	6821	|gnl|PID|d101323	|YqhU |Bacillus subtilis|	65	50	576
10	2	1873	1397	|gi|1163111	|ORF-1 |Streptococcus pneumoniae|	65	54	477
16	3	1428	2222	|gnl|PID|e325010	|hypothetical protein |Bacillus subtilis|	65	45	795
21	4	3815	3357	|gnl|PID|e314910	|hypothetical protein |Staphylococcus sciuri|	65	40	459
22	34	25776	26384	|gi|1123030	|CpxA |Actinobacillus pleuropneumoniae|	65	42	609
43	2	1648	290	|gi|1044826	|F14E5.1 |Caenorhabditis elegans|	65	38	1359
48	13	10062	10856	|gi|1573390	|hypothetical |Haemophilus influenzae|	65	45	795
48	22	17521	16883	|gi|1573391	|hypothetical |Haemophilus influenzae|	65	37	639
48	25	19027	18533	|gnl|PID|e264484	|YCR020c, len:215 |Saccharomyces cerevisiae|	65	38	495
49	3	3856	5334	|gi|1480429	|putative transcriptional regulator |Bacillus stearothermophilus|	65	32	1479
50	6	5337	4519	|gi|171963	|tRNA isopentenyl transferase |Saccharomyces cerevisiae|	65	42	819
52	15	14728	15588	|gi|1499745	|M. jannaschii predicted coding region MJ0912 |Methanococcus jannaschii|	65	46	861
59	7	3963	4745	|gi|496514	|orf zeta |Streptococcus pyogenes|	65	42	783
68	3	2500	3483	|gi|887824	|ORF_o310 |Escherichia coli|	65	46	984
69	3	2171	1077	|gnl|PID|e311453	|unknown |Bacillus subtilis|	65	42	1095
69	7	6029	5325	|gi|809660	|deoxyribose-phosphate aldolase |Bacillus subtilis|	65	55	705
71	5	8536	9783	|gi|1573224	|glycosyl transferase lgtC (GP:U14554_4) |Haemophilus influenzae|	65	42	1248
72	8	7664	8527	|gnl|PID|e267589	|Unknown, highly similar to several spermidine synthases |Bacillus subtilis|	65	39	864

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
284	1	1	900	gi|559861	clyH (Plasmid pAD1)	65	36	900
304	1	2	574	gnl|PID|e290934	unknown (Mycobacterium tuberculosis)	65	52	573
315	1	2	1483	gi|790694	mannuronan C-5-epimerase (Azotobacter vinelandii)	65	57	1482
320	1	3	569	gnl|PID|d102048	K. aerogenes, histidine utilization repressor; P12380 (199) DNA binding (Bacillus subtilis)	65	46	567
358	1	1	309	gnl|PID|e323508	YloS protein (Bacillus subtilis)	65	55	309
2	7	7571	6696	gi|1498753	nicotinate-nucleotide pyrophosphorylase (Rhodospirillum rubrum)	64	47	876
6	6	5924	6802	gnl|PID|d101111	methionine aminopeptidase (Synechocystis sp.)	64	52	879
8	4	3417	3686	gi|1045935	DNA helicase II (Mycoplasma genitalium)	64	58	270
11	4	3249	2689	gnl|PID|e265529	OrfB (Streptococcus pneumoniae)	64	46	561
15	7	6504	7145	gi|1762328	Ycr59c/Yig2 homolog (Bacillus subtilis)	64	45	642
22	11	9548	9895	gnl|PID|d100581	unknown (Bacillus subtilis)	64	38	348
22	10	22503	23174	gi|289260	comE ORF1 (Bacillus subtilis)	64	44	672
26	7	14375	14199	gi|409286	bmrU (Bacillus subtilis)	64	30	177
27	2	1510	1334	gi|40795	DdeI methylase (Desulfovibrio vulgaris)	64	51	177
29	2	614	297	gi|2326168	type VII collagen (Mus musculus)	64	50	318
35	2	368	721	pir|JC1151|JC11	hypothetical 20.3K protein (insertion sequence IS1131) - Agrobacterium tumefaciens (strain PO22) plasmid Ti	64	50	354
40	1	3	449	gi|46970	epiD gene product (Staphylococcus epidermidis)	64	41	447
40	7	4683	4976	gnl|PID|e325792	(AJ000005) glucose kinase (Bacillus megaterium)	64	45	294
45	7	8068	6920	gnl|PID|d102036	subunit of ADP-glucose pyrophosphorylase (Bacillus stearothermophilus)	64	40	1149
51	2	301	1059	gi|43985	nifS-like gene (Lactobacillus delbrueckii)	64	54	759
51	13	15251	18397	gi|2293260	(AF008220) DNA-polymerase III alpha-chain (Bacillus subtilis)	64	46	3147
53	3	1157	555	gi|1574292	hypothetical (Haemophilus influenzae)	64	47	603
58	2	4236	1606	gi|1573826	alanyl-tRNA synthetase (alaS) (Haemophilus influenzae)	64	51	2631
66	1	3	1259	gi|895749	putative cellobiose phosphotransferase enzyme II'' (Bacillus subtilis)	64	42	1257
68	5	5213	6556	gi|436965	(malA) gene products (Bacillus stearothermophilus)	64	47	1344
69	6	5356	4949	gnl|PID|d101316	Cdd (Bacillus subtilis)	64	52	408

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
74	4	6948	5038	gi|726480	L-glutamine-D-fructose-6-phosphate amidotransferase (Bacillus subtilis)	64	50	1911
75	3	1283	1465	bbs|133379	TLS-CHOP=fusion protein(CHOP=C/EBP transcription factor, TLS=nuclear RNA-binding protein) (human, myxoid liposarcomas cells, Peptide Mutant, 462 aa) (Homo sapiens)	64	57	183
81	13	14016	14231	gi|143175	methanol dehydrogenase alpha-10 subunit (Bacillus sp.)	64	35	216
83	22	21851	22090	gnl|PID|d101315	YqfA (Bacillus subtilis)	64	44	240
87	11	10046	9300	gnl|PID|e323505	putative Ptcl protein (Bacillus subtilis)	64	43	747
98	7	5032	5706	gnl|PID|e233880	hypothetical protein (Bacillus subtilis)	64	38	675
105	1	2	1276	gi|1657503	similar to S. aureus mercury(II) reductase (Escherichia coli)	64	45	1275
113	7	5136	6410	gnl|PID|d101119	NifS (Synechocystis sp.)	64	50	1275
119	1	2	1297	gnl|PID|e320520	hypothetical protein (Natronobacterium pharaonis)	64	37	1296
123	3	1125	2156	gnl|PID|e253284	ORF YDL244w (Saccharomyces cerevisiae)	64	40	1032
124	5	2331	1780	gnl|PID|d101884	hypothetical protein (Synechocystis sp.)	64	50	552
129	4	3467	2709	gnl|PID|d101314	YqeU (Bacillus subtilis)	64	52	759
131	1	152	3	gi|1377841	unknown (Bacillus subtilis)	64	42	150
137	11	7196	7549	pir|JC1151|JC11	hypothetical 20.3K protein (insertion sequence ISI131) - Agrobacterium tumefaciens (strain PO22) plasmid Ti	64	50	354
139	3	3226	2651	gi|2293301	(AF008220) YtqB (Bacillus subtilis)	64	44	576
146	10	6730	5648	gi|1322245	mevalonate pyrophosphate decarboxylase (Rattus norvegicus)	64	45	1083
147	1	2	1018	gnl|PID|e137033	unknown gene product (Lactobacillus leichmannii)	64	46	1017
148	11	8430	8783	gi|2130630	(AF000430) dynamin-like protein (Homo sapiens)	64	28	354
156	7	4313	3612	gnl|PID|d102050	transmembrane (Bacillus subtilis)	64	31	702
157	4	1299	2114	gnl|PID|d100892	homologous to Gln transport system permease proteins (Bacillus subtilis)	64	43	816
162	6	5880	6362	gi|517204	ORF1, putative 42 kDa protein (Streptococcus pyogenes)	64	58	483
164	13	9707	8769	gnl|PID|d100964	homologue of ferric anguibactin transport system permerase protein FatD of V. anguillarum (Bacillus subtilis)	64	40	939
175	5	3906	4598	gi|534045	antiterminator (Bacillus subtilis)	64	39	693
189	10	6154	6507	gi|581307	response regulator (Lactobacillus plantarum)	64	33	354
191	4	3519	2863	gi|149520	phosphoribosyl anthranilate isomerase (Lactococcus lactis)	64	46	657

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
202	1	76	1140	gnl|PID|e293806	O-acetylhomoserine sulfhydrylase (Leptospira meyeri)	64	47	1065
224	1	234	1571	gi|1573393	collagenase (prtC) (Haemophilus intluenzae)	64	42	1338
231	3	291	647	gi|40174	ORF X (Bacillus subtilis)	64	43	357
253	3	709	1089	pir|JC1151|JC11	hypothetical 20.3K protein (insertion sequence IS1131) - Agrobacterium tumefaciens (strain PO22) plasmid Ti	64	50	381
265	1	820	2	gi|1377832	unknown (Bacillus subtilis)	64	31	819
297	1	1	660	gi|1590871	collagenase (Methanococcus jannaschii)	64	48	660
328	1	263	21	gi|992651	Gln4p (Saccharomyces cerevisiae)	64	41	243
5	4	8730	8098	gi|556885	Unknown (Bacillus subtilis)	63	48	633
10	6	5178	4483	gi|1573101	hypothetical (Haemophilus influenzae)	63	40	696
12	11	9324	9902	gi|806536	membrane protein (Bacillus acidopullulyticus)	63	42	579
15	10	8897	9187	gi|722339	unknown (Acetobacter xylinum)	63	40	291
17	2	1031	309	gnl|PID|e217602	PlnU (Lactobacillus plantarum)	63	32	723
18	8	7778	6975	gi|1377843	unknown (Bacillus subtilis)	63	45	804
26	4	9780	7078	gi|142440	ATP-dependent nuclease (Bacillus subtilis)	63	46	2703
29	5	3488	4192	gi|1377829	unknown (Bacillus subtilis)	63	35	705
34	11	8830	7988	gnl|PID|d101198	ORF8 (Enterococcus faecalis)	63	45	843
35	3	1187	876	gi|722339	unknown (Acetobacter xylinum)	63	39	312
48	15	12509	11691	gi|1573389	hypothetical (Haemophilus influenzae)	63	41	819
51	11	12719	12189	gi|142450	ahrC protein (Bacillus subtilis)	63	35	531
55	4	3979	5022	gi|1708640	YeaB (Bacillus subtilis)	63	41	1044
55	15	13669	14670	gnl|PID|e311502	thioredoxine reductase (Bacillus subtilis)	63	44	1002
68	10	9242	8919	sp|P37686|YIAY_	HYPOTHETICAL 40.2 KD PROTEIN IN AVTA-SELB INTERGENIC REGION (F382).	63	40	324
86	7	6554	5685	gi|1574382	lic-1 operon protein (licD) (Haemophilus influenzae)	63	41	870
88	8	6085	5180	gi|2098719	putative fimbrial-associated protein (Actinomyces naeslundii)	63	43	906
96	8	5858	6484	gi|1052803	orf1gyrb gene product (Streptococcus pneumoniae)	63	38	627
100	1	240	1940	gi|7171	fucosidase (Dictyostelium discoideum)	63	36	1701

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
104	4	3063	5765	gi|144985	phosphoenolpyruvate carboxylase (Corynebacterium glutamicum)	63	46	2703
106	8	9189	8554	gi|533099	endonuclease III (Bacillus subtilis)	63	45	636
122	6	4704	4886	gnl|PID|d101139	transposase (Synechocystis sp.)	63	39	183
128	7	4517	5203	gnl|PID|d101434	orf2 (Methanobacterium thermoautotrophicum)	63	50	687
137	4	963	1547	gi|472920	v-type Na-ATPase (Enterococcus hirae)	63	27	585
142	7	4100	4585	gnl|PID|e313025	hypothetical protein (Bacillus subtilis)	63	44	486
159	5	1741	2571	gi|1787043	(AE000184) f271; This 271 aa orf is 24 pct identical (16 gaps) to 265 residues of an approx. 272 aa protein YIDA_ECOLI SW: P09997 (Escherichia coli)	63	39	831
171	12	8803	14406	gnl|PID|e324918	IgA1 protease (Streptococcus sanguis)	63	48	5604
177	1	3	347	gi|1773150	hypothetical 14.8kd protein (Escherichia coli)	63	34	345
178	2	423	917	gi|722339	unknown (Acetobacter xylinum)	63	41	495
178	3	794	1012	gi|1591582	cobalamin biosynthesis protein N (Methanococcus jannaschii)	63	36	219
195	1	1377	175	gnl|PID|e324217	ftsQ (Enterococcus hirae)	63	33	1203
234	5	1739	1527	gi|1591582	cobalamin biosynthesis protein N (Methanococcus jannaschii)	63	36	213
249	3	81	257	gi|1000453	TreR (Bacillus subtilis)	63	41	177
283	1	127	1347	gi|396486	ORF8 (Bacillus subtilis)	63	44	1221
293	3	2804	3466	gi|722339	unknown (Acetobacter xylinum)	63	37	663
311	1	905	486	gi|1877424	UDP-galactose 4-epimerase (Streptococcus mutans)	63	46	420
324	1	2	556	gi|1477741	histidine periplasmic binding protein P29 (Campylobacter jejuni)	63	36	555
365	1	219	13	gi|2252843	(AF013293) No definition line found (Arabidopsis thaliana)	63	33	207
382	1	88	378	gi|722339	unknown (Acetobacter xylinum)	63	40	291
385	3	364	158	gi|2252843	(AF013293) No definition line found (Arabidopsis thaliana)	63	33	207
2	1	2495	288	gnl|PID|e325007	penicillin-binding protein (Bacillus subtilis)	62	42	2208
3	23	23374	24231	gnl|PID|e254993	hypothetical protein (Bacillus subtilis)	62	35	858
6	16	14320	13193	gnl|PID|e349614	nifS-like protein (Mycobacterium leprae)	62	37	1128
7	8	6819	7232	gnl|PID|d101324	YqhY (Bacillus subtilis)	62	32	414
7	19	15466	14207	gnl|PID|d101804	beta ketoacyl-acyl carrier protein synthase (Synechocystis sp.)	62	43	1260

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
7	21	17155	16229	gnl|PID|e323514	putative FabD protein (Bacillus subtilis)	62	46	927
7	24	19526	18519	gi|1276434	beta-ketoacyl-ACP synthase III (Cuphea wrightii)	62	37	1008
12	7	5904	4702	gi|1573768	A/G-specific adenine glycosylase (mutY) (Haemophilus influenzae)	62	43	1203
12	9	8032	8793	gi|1591587	pantothenate metabolism flavoprotein (Methanococcus jannaschii)	62	33	762
15	11	9678	9328	pir|JC1151|JC11	hypothetical 20.3K protein (insertion sequence ISI131) - Agrobacterium tumefaciens (strain PO22) plasmid Ti	62	43	351
17	4	2609	2442	gi|1591081	M. jannaschii predicted coding region MJ0374 (Methanococcus jannaschii)	62	43	168
17	5	3053	2835	gi|149570	role in the expression of lactacin F, part of the laf operon (Lactobacillus sp.)	62	44	219
22	10	8627	9538	gnl|PID|d100580	similar to B. subtilis DnaH (Bacillus subtilis)	62	43	912
30	3	865	2043	gi|2314379	(AE000627) ABC transporter, ATP-binding protein (yhcG) (Helicobacter pylori)	62	43	1179
31	5	2235	1636	gi|413976	ipa-52r gene product (Bacillus subtilis)	62	44	600
38	11	5689	6123	gi|148231	o251 (Escherichia coli)	62	34	435
40	17	14272	13328	gnl|PID|d101904	hypothetical protein (Synechocystis sp.)	62	43	945
42	1	3	311	gi|1146182	putative (Bacillus subtilis)	62	41	309
44	2	1267	4005	gi|1786952	(AE000176) o877; 100 pct identical to the first 86 residues of the 100 aa hypothetical protein fragment YBGB_ECOLI SW: P54746 (Escherichia coli)	62	43	2739
48	12	9732	9304	gi|662920	repressor protein (Enterococcus hirae)	62	32	429
51	8	5664	7181	gnl|PID|e301153	StySKI methylase (Salmonella enterica)	62	44	1518
52	3	2791	2099	gi|1183886	integral membrane protein (Bacillus subtilis)	62	41	693
55	16	15702	14704	gnl|PID|e313028	hypothetical protein (Bacillus subtilis)	62	40	999
59	6	3418	3984	gi|2065483	unknown (Lactococcus lactis lactis)	62	32	567
63	5	4997	4809	gi|149771	pilin gene inverting protein (PivML) (Moraxella lacunata)	62	28	189
70	14	10002	10739	gi|992977	bplG gene product (Bordetella pertussis)	62	45	738
71	13	18790	20382	gi|1280135	coded for by C. elegans cDNA cm21e6; coded for by C. elegans cDNA cm01e2; similar to melibiose carrier protein (thiomethylgalactoside permease II) (Caenorhabditis elegans)	62	62	1593
71	28	32217	32768	gnl|PID|d101312	YqeG (Bacillus subtilis)	62	35	552
74	7	11666	10383	gi|1552753	hypothetical (Escherichia coli)	62	38	1284

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
80	8	9370	9609	|gnl|PID|d102002	(AB001488) FUNCTION UNKNOWN. [Bacillus subtilis]	62	46	240
97	10	9068	7041	|gi|882463	|protein-N(pi)-phosphohistidine-sugar phosphotransferase [Escherichia coli]	62	42	2028
98	4	2306	3268	|gnl|PID|d101496	|BraE (integral membrane protein) [Pseudomonas aeruginosa]	62	42	963
102	3	2823	3539	|gnl|PID|e313010	|hypothetical protein [Bacillus subtilis]	62	24	717
103	3	2795	1242	|gnl|PID|d102049	|H. influenzae hypothetical ABC transporter; P44808 (974) [Bacillus subtilis]	62	41	1554
111	2	2035	3462	|gi|581297	|NisP [Lactococcus lactis]	62	44	1428
112	4	3154	4080	|gi|1574379	|lic-1 operon protein (licA) [Haemophilus influenzae]	62	39	927
112	6	4939	5649	|gi|1574381	|lic-1 operon protein (licC) [Haemophilus influenzae]	62	39	711
124	3	1137	721	|gi|1573024	|anaerobic ribonucleoside-triphosphate reductase (nrdD) [Haemophilus influenzae]	62	45	417
124	6	3162	2329	|gi|609076	|leucyl aminopeptidase [Lactobacillus delbrueckii]	62	40	834
126	7	11073	7516	|gnl|PID|d101163	|ORF4 [Bacillus subtilis]	62	38	3558
129	6	4983	4540	|pir|S41509|S415	|zinc finger protein EF6 - Chilo iridescent virus	62	48	444
131	7	4510	4103	|gi|1857245	|unknown [Lactococcus lactis]	62	42	408
149	2	1923	2579	|gi|1592142	|ABC transporter, probable ATP-binding subunit [Methanococcus jannaschii]	62	41	657
149	7	5360	6055	|gnl|PID|e323508	|YloS protein [Bacillus subtilis]	62	40	696
156	1	450	238	|gnl|PID|e254644	|membrane protein [Streptococcus pneumoniae]	62	40	213
156	6	3606	2935	|gnl|PID|d102050	|transmembrane [Bacillus subtilis]	62	37	672
171	2	1779	2291	|gi|43941	|EIII-B Sor PTS [Klebsiella pneumoniae]	62	35	513
172	2	385	723	|gi|895750	|putative cellobiose phosphotransferase enzyme III [Bacillus subtilis]	62	39	339
173	3	2599	893	|gi|1591732	|cobalt transport ATP-binding protein O [Methanococcus jannaschii]	62	42	1707
179	2	492	1754	|gi|1574071	|H. influenzae predicted coding region HI1038 [Haemophilus influenzae]	62	38	1263
181	6	2856	3707	|gi|1777435	|LacT [Lactobacillus casei]	62	42	852
185	2	2074	311	|gi|2182397	|(AE000073) Y4fN [Rhizobium sp. NGR234]	62	41	1764
200	2	1061	1984	|gi|450566	|transmembrane protein [Bacillus subtilis]	62	37	924
202	3	2583	3473	|gi|42219	|P35 gene product (AA 1 - 314) [Escherichia coli]	62	41	891
210	3	1374	1565	|gi|49315	|ORF1 gene product [Bacillus subtilis]	62	45	192

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match accession	match gene name	% sim	% ident	length (nt)
211	1	3	971	gi|147402	mannose permease subunit III-Man (Escherichia coli)	62	43	969
223	2	1495	1034	gnl|PID|d101190	ORF2 (Streptococcus mutans)	62	41	462
228	1	34	909	gi|530063	glycerol uptake facilitator (Streptococcus pneumoniae)	62	44	876
234	2	90	917	gi|2293259	(AF008220) YtqI (Bacillus subtilis)	62	38	828
282	5	1765	1487	gnl|PID|e276475	galactokinase (Arabidopsis thaliana)	62	33	279
375	1	1	159	gi|1674231	(AE000052) Mycoplasma pneumoniae, hypothetical protein homolog; similar to Swiss-Prot Accession Number P35155, from B. subtilis (Mycoplasma pneumoniae)	62	40	159
385	5	584	357	gi|1573353	outer membrane integrity protein (tolA) (Haemophilus influenzae)	62	47	228
3	19	18550	19269	gi|606162	ORF_f229 (Escherichia coli)	61	41	720
7	4	2725	3225	gi|2114425	similar to Synechocystis sp. hypothetical protein, encoded by GenBank Accession Number D64006 (Bacillus subtilis)	61	42	501
17	6	3326	3054	gi|149569	lactacin F (Lactobacillus sp.)	61	43	273
44	3	4061	4957	gnl|PID|d101068	xylose repressor (Synechocystis sp.)	61	38	897
54	11	8388	7234	gnl|PID|d101329	YqjH (Bacillus subtilis)	61	42	1155
57	6	3974	6037	gnl|PID|d101316	YqfK (Bacillus subtilis)	61	42	2064
58	5	7356	6565	sp|P45169|POTC_	SPERMIDINE/PUTRESCINE TRANSPORT SYSTEM PERMEASE PROTEIN POTC.	61	34	792
67	1	3	692	gi|537108	ORF_f254 (Escherichia coli)	61	46	690
68	9	8816	7890	gi|19501	pPLZ12 gene product (AA 1-184) (Lupinus polyphyllus)	61	41	927
70	15	10737	12008	gi|992976	bplF gene product (Bordetella pertussis)	61	44	1272
72	11	9759	10202	gnl|PID|d101833	carboxynorspermidine decarboxylase (Synechocystis sp.)	61	36	444
76	8	7881	7003	gnl|PID|d100305	farnesyl diphosphate synthase (Bacillus stearothermophilus)	61	45	879
87	4	4914	3697	gi|528991	unknown (Bacillus subtilis)	61	42	1218
87	13	12311	11361	gi|1789683	(AE000407) methionyl-tRNA formyltransferase (Escherichia coli)	61	44	951
91	2	731	2989	gi|537080	ribonucleoside triphosphate reductase (Escherichia coli)	61	45	2259
105	3	2711	3499	gnl|PID|d101851	hypothetical protein (Synechocystis sp.)	61	44	789
115	6	7960	6478	gi|895747	putative cel operon regulator (Bacillus subtilis)	61	36	1491
123	8	7181	8518	gi|1209527	protein histidine kinase (Enterococcus faecalis)	61	40	1338

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match accession	match gene name	% sim	% ident	length (nt)
126	6	7525	6725	gi|1787043	(AE000184) f271; This 271 aa orf is 24 pct identical (16 gaps) to 265 residues of an approx. 272 aa protein YIDA_ECOLI SW: P09997 (Escherichia coli)	61	38	801
128	1	1	639	gnl|PID|d101328	YqiY (Bacillus subtilis)	61	41	639
139	7	4794	5054	gi|1022726	unknown (Staphylococcus haemolyticus)	61	41	261
139	9	12632	5913	gnl|PID|e270014	beta-galactosidase (Thermoanaerobacter ethanolicus)	61	41	6720
141	1	2552	42	gi|520541	penicillin-binding proteins 1A and 1B (Bacillus subtilis)	61	42	2511
148	16	12125	11424	gi|1552743	tetrahydrodipicolinate N-succinyltransferase (Escherichia coli)	61	42	702
162	3	4112	3456	gnl|PID|d101829	phosphoglycolate phosphatase (Synechocystis sp.)	61	30	657
172	3	727	1077	gnl|PID|d102048	B. subtilis, cellobiose phosphotransferase system, celA; P46318 (220) (Bacillus subtilis)	61	44	351
177	3	1101	1772	gnl|PID|d100574	unknown (Bacillus subtilis)	61	43	672
202	2	1278	2585	gi|1045831	hypothetical protein (GB:L18965_6) (Mycoplasma genitalium)	61	36	1308
224	3	2782	3144	gi|1591144	M. jannaschii predicted coding region MJ0440 (Methanococcus jannaschii)	61	30	363
225	4	3195	3766	gi|1552774	hypothetical (Escherichia coli)	61	40	372
249	2	212	802	gi|1000453	TreR (Bacillus subtilis)	61	42	591
254	2	843	484	gnl|PID|d100417	ORF120 (Escherichia coli)	61	36	360
257	1	3	350	gnl|PID|e255315	unknown (Mycobacterium tuberculosis)	61	42	348
293	4	3971	3657	pir|JC1151|JC11	hypothetical 20.3K protein (insertion sequence IS1131) - Agrobacterium tumefaciens (strain PO22) plasmid Ti	61	45	315
301	1	949	17	gi|2291209	(AF016424) contains similarity to acyltransferases (Caenorhabditis elegans)	61	33	933
373	1	1066	287	gi|393396	Tb-292 membrane associated protein (Trypanosoma brucei subgroup)	61	38	780
3	24	24473	24955	gi|537093	ORF_o153b (Escherichia coli)	60	27	483
6	5	4636	5739	gi|2293258	(AF008220) YtoI (Bacillus subtilis)	60	35	1104
6	12	11936	11187	gi|293017	ORF3 (put.); putative (Lactococcus lactis)	60	44	750
17	13	6708	6484	gi|149569	lactacin F (Lactobacillus sp.)	60	32	225
18	7	6977	5670	gi|1788140	(AE000278) o481; This 481 aa orf is 35 pct identical (19 gaps) to 309 residues of an approx. 856 aa protein NOL1_HUMAN SW: P46087 (Escherichia coli)	60	43	1308
20	15	15870	17167	gnl|PID|d100584	unknown (Bacillus subtilis)	60	44	1290

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
22	1	1	243	|gnl|PID|d102050	transmembrane [Bacillus subtilis]	60	36	243
32	10	8296	8964	|gi|2293275	(AF008220) YtaG [Bacillus subtilis]	60	37	669
38	15	8837	9697	|gi|40023	B.subtilis genes rpmH, rnpA, 50kd, gidA and gidB [Bacillus subtilis]	60	35	861
43	6	8610	5944	|gi|171787	protein kinase 1 [Saccharomyces cerevisiae]	60	36	2667
44	1	1	1269	|gnl|PID|e235823	unknown [Schizosaccharomyces pombe]	60	44	1269
45	10	11138	10368	|gi|397488	1,4-alpha-glucan branching enzyme [Bacillus subtilis]	60	43	771
48	19	15766	14378	|gnl|PID|e205173	orf1 [Lactobacillus helveticus]	60	39	1389
48	21	16727	16951	|gnl|PID|d102041	(AB002668) unnamed protein product [Haemophilus actinomycetemcomitans]	60	32	225
50	1	2	898	|gnl|PID|e246537	ORF286 protein [Pseudomonas stutzeri]	60	31	897
62	2	638	1177	|gnl|PID|d100587	unknown [Bacillus subtilis]	60	42	540
68	4	3590	5203	|gi|157358	H. influenzae predicted coding region HI0594 [Haemophilus influenzae]	60	36	1614
70	11	5781	6182	|gnl|PID|d102014	(AB001488) SIMILAR TO YDFR GENE PRODUCT OF THIS ENTRY (YDFR_BACSU). [Bacillus subtilis]	60	33	402
70	12	6343	8133	|gnl|PID|e324970	hypothetical protein [Bacillus subtilis]	60	38	1791
71	8	11701	14157	|gi|580866	ipa-12d gene product [Bacillus subtilis]	60	33	2457
74	8	12509	11664	|gnl|PID|d101832	phosphatidate cytidylyltransferase [Synechocystis sp.]	60	45	846
76	4	4116	3367	|gi|2352096	orf; similar to serine/threonine protein phosphatase [Fervidobacterium islandicum]	60	39	750
80	4	7372	7665	|gi|1786420	(AE000131) f86; 100 pct identical to GB: ECODINJ_6 ACCESSION: D38582 [Escherichia coli]	60	30	294
81	6	4073	4522	|gi|147402	mannose permease subunit III-Man [Escherichia coli]	60	35	450
86	1	940	155	|gi|143177	putative [Bacillus subtilis]	60	26	786
92	1	1	192	|gi|396348	homoserine transsuccinylase [Escherichia coli]	60	45	192
93	14	10619	9384	|gi|1788389	(AE000297) o464; This 464 aa orf is 33 pct identical (9 gaps) to 331 residues of an approx. 416 aa protein HTRC_NEIGO SW: P43505 [Escherichia coli]	60	27	1236
94	5	5548	8121	|gnl|PID|e329895	(AJ000496) cyclic nucleotide-gated channel beta subunit [Rattus norvegicus]	60	50	2574
97	7	5396	4533	|gi|1591396	transketolase' [Methanococcus jannaschii]	60	43	864
102	2	2081	2833	|gnl|PID|e320929	hypothetical protein [Mycobacterium tuberculosis]	60	43	753

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
106	9	9773	9183	|gnl|PID|e334782	YlbN protein (Bacillus subtilis)	60	31	591
113	8	6361	6837	|gi|466875	nifU; B1496_C1_157 (Mycobacterium leprae)	60	43	477
115	2	2755	524	|gnl|PID|e328143	(AJ000332) Glucosidase II (Homo sapiens)	60	32	2232
122	7	4763	5068	|gnl|PID|d101876	transposase (Synechocystis sp.)	60	39	306
127	8	4510	5283	|gi|1777938	Pgm (Treponema pallidum)	60	38	774
138	4	3082	2672	|gnl|PID|e325196	hypothetical protein (Bacillus subtilis)	60	36	411
139	1	177	4	|gnl|PID|d100680	ORF (Thermus thermophilus)	60	39	174
139	11	14520	13009	|gi|537145	ORF_f437 (Escherichia coli)	60	30	1512
140	2	2592	1249	|gi|1209527	protein histidine kinase (Enterococcus faecalis)	60	37	1344
141	1	210	1049	|gi|463181	E5 ORF from bp 3842 to 4081; putative (Human papillomavirus type 33)	60	34	840
141	5	5368	6405	|gi|145362	tyrosine-sensitive DAHP synthase (aroF) (Escherichia coli)	60	41	1038
142	6	3558	4049	|gi|600711	putative (Bacillus subtilis)	60	37	492
148	10	7742	8713	|gnl|PID|e313022	hypothetical protein (Bacillus subtilis)	60	27	972
153	5	3667	4278	|gi|2293322	(AF008220) branch-chain amino acid transporter (Bacillus subtilis)	60	42	612
155	1	1413	748	|gi|2104504	putative UDP-glucose dehydrogenase (Escherichia coli)	60	40	666
158	3	3116	2472	|gnl|PID|d100872	a negative regulator of pho regulon (Pseudomonas aeruginosa)	60	37	645
159	3	778	1386	|gnl|PID|e308090	product highly similar to Bacillus anthracis CapA protein (Bacillus subtilis)	60	48	609
163	7	8049	8468	|gnl|PID|d101313	YqeN (Bacillus subtilis)	60	38	420
170	3	4130	2688	|gi|1574179	H. influenzae predicted coding region HI1244 (Haemophilus influenzae)	60	39	1443
171	7	4717	5901	|gi|606076	ORF_o384 (Escherichia coli)	60	44	1185
183	3	2440	2135	|gi|1877427	repressor (Streptococcus pyogenes phage T12)	60	38	306
191	10	9444	8428	|gi|415664	catabolite control protein (Bacillus megaterium)	60	42	1017
200	1	139	1083	|gi|438462	transmembrane protein (Bacillus subtilis)	60	37	945
201	3	3895	1928	|gi|475112	enzyme IIabc (Pediococcus pentosaceus)	60	39	1968
214	15	10930	10439	|gi|1573407	hypothetical (Haemophilus influenzae)	60	39	492
218	4	2145	2363	|gi|608520	myosin heavy chain kinase A (Dictyostelium discoideum)	60	31	219

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
226	4	2518	2351	gi|437705	hyaluronidase [Streptococcus pneumoniae]	60	53	168
242	1	725	3	gi|43938	Sor regulator [Klebsiella pneumoniae]	60	41	723
245	1	1	288	gi|304897	EcoE type I restriction modification enzyme M subunit [Escherichia coli]	60	56	288
251	1	905	45	gi|671632	unknown [Staphylococcus aureus]	60	36	861
259	1	969	82	gi|153794	rgg [Streptococcus gordonii]	60	32	888
260	2	1492	1662	pir|S31840|S318	probable transposase - Bacillus stearothermophilus	60	26	171
274	1	836	96	gi|1592173	N-ethylammeline chlorohydrolase [Methanococcus jannaschii]	60	40	741
308	1	463	2	gi|1787397	(AE000214) o157 [Escherichia coli]	60	43	462
318	1	3	308	gnl|PID|e137594	xerC recombinase [Lactobacillus leichmannii]	60	42	306
344	1	73	522	gi|509672	repressor protein [Bacteriophage Tuc2009]	60	32	450
5	1	576	4	gi|2293147	(AF008220) YtxH [Bacillus subtilis]	59	31	573
7	22	18140	17142	gnl|PID|e280724	unknown [Mycobacterium tuberculosis]	59	39	999
10	1	1413	4	gi|1353880	sialidase L [Macrobdella decora]	59	41	1410
15	6	6463	5156	gi|580841	F1 [Bacillus subtilis]	59	35	1308
22	2	479	1393	gi|142469	als operom regulatory protein [Bacillus subtilis]	59	34	915
22	5	2698	4614	gnl|PID|e280623	PCPA [Streptococcus pneumoniae]	59	44	1917
30	1	208	558	gnl|PID|e233868	hypothetical protein [Bacillus subtilis]	59	37	351
30	4	3678	2455	gnl|PID|e202290	unknown [Lactobacillus sake]	59	33	1224
35	13	12201	11071	gnl|PID|e238664	hypothetical protein [Bacillus subtilis]	59	35	1131
35	14	13288	12182	gi|1657647	Cap8H [Staphylococcus aureus]	59	39	1107
36	18	18076	17897	gi|1500535	M. jannaschii predicted coding region MJ1635 [Methanococcus jannaschii]	59	33	180
38	12	6172	7137	gi|2293239	(AF008220) YtxK [Bacillus subtilis]	59	34	966
42	3	1952	3361	gi|1684845	pinin [Canis familiaris]	59	40	1410
50	3	2678	1728	gnl|PID|d101329	YqjK [Bacillus subtilis]	59	41	951
56	5	1870	2388	gnl|PID|e137594	xerC recombinase [Lactobacillus leichmannii]	59	41	519
61	6	6812	5628	gnl|PID|e311516	aminotransferase [Bacillus subtilis]	59	40	1185
67	5	2382	3023	gi|1146190	2-keto-3-deoxy-6-phosphogluconate aldolase [Bacillus subtilis]	59	36	642

TABLE 2

S pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
69	10	8567	8899	gi|1573628	antothenate kinase (coaA) (Haemophilus influenzae)	59	38	333
87	12	11383	10055	gnl|PID|e323504	putative Fmu protein (Bacillus subtilis)	59	44	1329
113	14	13927	15894	gi|1673731	(AE000010) Mycoplasma pneumoniae, fructose-permease IIBC component; similar to Swiss-Prot Accession Number P20966, from E. coli (Mycoplasma pneumoniae)	59	43	1968
115	8	8766	8521	gi|1590886	M. jannaschii predicted coding region MJ0110 (Methanococcus jannaschii)	59	38	246
119	2	1966	1526	gnl|PID|e209005	homologous to ORF2 in nrdEF operons of E.coli and S.typhimurium (Lactococcus lactis)	59	43	441
128	17	13438	13178	gnl|PID|e279632	unknown (Mycobacterium tuberculosis)	59	38	261
140	22	23903	23388	gi|482922	protein with homology to pail repressor of B.subtilis (Lactobacillus delbrueckii)	59	40	516
148	13	9697	9014	gnl|PID|d102005	(AB001488) FUNCTION UNKNOWN, SIMILAR PRODUCT IN H. INFLUENZAE AND SYNECHOCYSTIS. (Bacillus subtilis)	59	32	684
149	10	7213	8244	gi|710422	cmp-binding-factor 1 (Staphylococcus aureus)	59	40	1032
164	9	6993	6013	gnl|PID|d100965	ferric anguibactin-binding protein precusor FatB of V. anguillarum (Bacillus subtilis)	59	41	981
164	12	8836	7823	gnl|PID|d100964	homologue of ferric anguibactin transport system permerase protein FatC of V. anguillarum (Bacillus subtilis)	59	35	1014
177	2	401	1072	gi|289759	coded for by C. elegans cDNA CE2G3 (GenBank:Z14728); putative (Caenorhabditis elegans)	59	40	672
177	7	3841	4200	gi|2313445	(AE000551) H. pylori predicted coding region HP0342 (Helicobacter pylori)	59	38	360
183	4	2768	2508	gi|509672	repressor protein (Bacteriophage Tuc2009)	59	50	261
186	6	3398	2820	gi|606080	ORF_o290; Geneplot suggests frameshift linking to o267, not found (Escherichia coli)	59	38	579
190	3	3120	1711	gi|1613768	histidine protein kinase (Streptococcus pneumoniae)	59	32	1410
194	2	1621	1019	gnl|PID|d100579	unknown (Bacillus subtilis)	59	40	603
198	7	5205	4306	gnl|PID|e313073	hypothetical protein (Bacillus subtilis)	59	38	900
220	5	4362	3958	gnl|PID|d101322	YqhL (Bacillus subtilis)	59	46	405
242	3	1573	2367	gi|1787045	(AE000184) f308; This 308 aa orf is 35 pct identical (35 gaps) to 305 residues of an approx. 296 aa protein PFLC_ECOLI SW: P32675 (Escherichia coli)	59	42	795
247	2	1154	1480	gi|40073	ORF107 (Bacillus subtilis)	59	39	327

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
256	1	868	2	|gnl|PID|d1001924	|hemolysin (Synechocystis sp.)	59	39	867
258	1	65	820	|gi|2246532	|ORF 73, contains large complex repeat CR 73 (Kaposi's sarcoma-associated herpesvirus)	59	20	756
270	1	386	1126	|gnl|PID|d102092	|YfnB (Bacillus subtilis)	59	40	741
281	1	552	166	|gi|666062	|putative (Lactococcus lactis)	59	31	387
309	1	3	479	|gi|405879	|yeiH (Escherichia coli)	59	38	477
363	1	2	1894	|gi|915208	|gastric mucin (Sus scrofa)	59	31	1893
387	2	425	84	|gi|160671	|S antigen precursor (Plasmodium falciparum)	59	44	342
5	6	11223	10465	|gnl|PID|d101812	|LumQ (Synechocystis sp.)	58	29	759
29	8	2098	3513	|gnl|PID|d100479	|Na+ -ATPase subunit J (Enterococcus hirae)	58	39	1416
30	5	4058	3651	|gi|39478	|ATP binding protein of transport ATPases (Bacillus firmus)	58	34	408
33	6	2983	2210	|gnl|PID|d101164	|unknown (Bacillus subtilis)	58	45	774
36	8	5316	6179	|gi|1518679	|orf (Bacillus subtilis)	58	32	864
43	5	5926	3971	|gi|1788150	|(AE000278) protease II (Escherichia coli)	58	37	1956
46	5	3704	5221	|gnl|PID|e267329	|Unknown (Bacillus subtilis)	58	42	1518
48	14	11722	11066	|gnl|PID|d101771	|thiamin biosynthetic bifunctional enzyme (Synechocystis sp.)	58	34	657
52	1	1229	3	|gnl|PID|d101291	|reductase (Pseudomonas aeruginosa)	58	35	1227
53	2	702	412	|gi|2313357	|(AE000545) cytochrome c biogenesis protein (ccdA) (Helicobacter pylori)	58	25	291
58	4	6586	5498	|gi|147329	|transport protein (Escherichia coli)	58	41	1089
69	5	4934	3807	|gnl|PID|e311492	|unknown (Bacillus subtilis)	58	41	1128
71	27	31357	32277	|gi|2408014	|hypothetical protein (Schizosaccharomyces pombe)	58	33	921
72	4	3586	2882	|gi|18694	|nodulin-21 (AA 1-201) (Glycine max)	58	34	705
74	3	4937	4230	|gi|2293252	|(AF008220) YtmO (Bacillus subtilis)	58	33	708
79	4	4594	3422	|gi|1217989	|ORF3 (Streptococcus pneumoniae)	58	44	1173
82	8	10585	8171	|gi|882711	|exonuclease V alpha-subunit (Escherichia coli)	58	38	2415
86	17	16017	15337	|gi|47642	|5-dehydroquinate hydrolyase (3-dehydroquinase) (Salmonella typhi)	58	32	681
97	2	931	560	|gi|153794	|rgg (Streptococcus gordonii)	58	32	372

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
108	2	358	2724	gi|537020	vacB gene product (Escherichia coli)	58	37	2367
111	5	4593	5240	gi|1592142	ABC transporter, probable ATP-binding subunit (Methanococcus jannaschii)	58	36	648
120	3	4421	5110	gnl|PID|d1013320	YqgX (Bacillus subtilis)	58	47	690
1	16	13131	12673	gi|662919	ORF U (Enterococcus hirae)	58	42	459
132	3	6174	4939	gi|1800301	macrolide-efflux determinant (Streptococcus pneumoniae)	58	35	1236
133	1	111	890	gnl|PID|e269488	Unknown (Bacillus subtilis)	58	36	780
160	11	8615	9865	gi|473901	ORF1 (Lactococcus lactis)	58	39	1251
161	6	6268	6849	gnl|PID|d101024	DJ-1 protein (Homo sapiens)	58	32	582
169	1	214	2	gnl|PID|d100447	translation elongation factor-3 (Chlorella virus)	58	31	213
187	1	487	2	gi|475114	regulatory protein (Pediococcus pentosaceus)	58	38	486
187	6	4384	4620	gi|167475	dessication-related protein (Craterostigma plantagineum)	58	55	237
190	2	1464	1640	gnl|PID|e246727	competence pheromone (Streptococcus gordonii)	58	38	177
192	2	2012	1344	gnl|PID|d100556	rat GCP360 (Rattus rattus)	58	44	669
206	1	1292	696	gnl|PID|e202579	product similar to WrbA (Lactobacillus sake)	58	35	597
216	2	2333	555	gnl|PID|e325036	hypothetical protein (Bacillus subtilis)	58	33	1779
217	5	5250	4321	gi|466474	cellobiose phosphotransferase enzyme II'' (Bacillus stearothermophilus)	58	38	930
217	7	5636	5106	gnl|PID|d102048	B. subtilis cellobiose phosphotransferase system celB; P46317 (998) transmembrane (Bacillus subtilis)	58	44	531
232	1	2	811	gi|1573777	cell division ATP-binding protein (ftsE) (Haemophilus influenzae)	58	39	810
264	1	2	715	gi|971330	NatA (Bacillus subtilis)	58	32	714
280	1	33	767	gi|1786187	(AE000111) hypothetical 29.6 kD protein in thrC-talB intergenic region (Escherichia coli)	58	31	735
306	1	845	3	gnl|PID|e334780	YlbL protein (Bacillus subtilis)	58	47	843
360	3	1556	1092	sp|P46351|YZGD_	HYPOTHETICAL 45.6 KD PROTEIN IN THIAMINASE I 5'REGION.	58	32	465
363	5	2160	1867	gi|160671	S antigen precursor (Plasmodium falciparum)	58	51	294
372	1	806	3	gi|393394	Tb-291 membrane associated protein (Trypanosoma brucei subgroup)	58	37	804
382	2	749	519	pir|JC1151|JC11	hypothetical 20.3K protein (insertion sequence IS1131) - Agrobacterium tumefaciens (strain PO22) plasmid Ti	58	41	231

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
3	9	8409	7471	gi|1499745	H. jannaschii predicted coding region MJ0912 (Methanococcus jannaschii)	57	38	939
10	10	7674	7507	gi|1737169	homologue to SKP1 (Arabidopsis thaliana)	57	30	168
11	1	2	412	gnl|PID|d1001139	ORF (Acetobacter pasteurianus)	57	42	411
31	4	2032	1388	gi|2293213	(AF008220) YtpR (Bacillus subtilis)	57	37	645
33	11	6931	6449	gnl|PID|e324949	hypothetical protein (Bacillus subtilis)	57	36	483
45	5	5446	5060	gi|1592204	phosphoserine phosphatase (Methanococcus jannaschii)	57	44	387
49	7	6523	7632	gi|155369	PTS enzyme-II fructose (Xanthomonas campestris)	57	35	1110
52	6	4520	6850	gi|1574144	single-stranded-DNA-specific exonuclease (recJ) (Haemophilus influenzae)	57	35	2331
53	5	2079	1795	gi|1843580	replicase-associated polyprotein (oat blue dwarf virus)	57	46	285
63	6	5312	4995	gi|2182608	(AE000094) Y4rJ (Rhizobium sp. NGR234)	57	39	318
72	15	13883	13059	gnl|PID|d100892	homologous to SwissProt:YIDA_ECOLI hypothetical protein (Bacillus subtilis)	57	40	825
79	2	2561	1815	gnl|PID|d100965	homologue of NADPH-flavin oxidoreductase Frp of V. harveyi (Bacillus subtilis)	57	44	747
82	9	9596	9763	gi|1206045	short region of similarity to glycerophosphoryl diester phosphodiesterases (Caenorhabditis elegans)	57	35	168
86	16	15371	14493	gi|1787983	(AE000264) o288; 92 pct identical (1 gaps) to 222 residues of fragment YDIB_ECOLI SW: P28244 (223 aa) (Escherichia coli)	57	34	879
93	3	1695	1177	gi|1500003	mutator mutT protein (Methanococcus jannaschii)	57	33	519
96	6	3026	4519	gi|559882	threonine synthase (Arabidopsis thaliana)	57	43	1494
99	14	17211	18212	gi|773349	BirA protein (Bacillus subtilis)	57	44	1002
112	8	7448	7903	gi|1591393	H. jannaschii predicted coding region MJ0678 (Methanococcus jannaschii)	57	30	456
113	16	18627	18328	pir|A45605|A456	mature-parasite-infected erythrocyte surface antigen MESA - Plasmodium falciparum	57	22	300
123	2	343	1110	pir|F64149|F641	hypothetical protein HI0355 - Haemophilus influenzae (strain Rd KW20)	57	38	768
123	4	2108	2884	gnl|PID|d102148	(AB001684) sulfate transport system permease protein (Chlorella vulgaris)	57	39	777
127	10	6477	5587	gi|1573082	nitrogenase C (nifC) (Haemophilus influenzae)	57	35	891
128	13	9251	9790	gi|153692	pneumolysin (Streptococcus pneumoniae)	57	38	540
131	4	2139	1363	gi|42081	nagD gene product (AA 1-250) (Escherichia coli)	57	36	777

TABLE 2

S pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
136	1	214	1221	bbs|148453	SpaA=endocarditis immunodominant antigen (Streptococcus sobrinus, MUCOB 263, Peptide, 1566 aa) (Streptococcus sobrinus)	57	44	1008
140	25	28701	26851	gi|505576	beta-glucoside permease (Bacillus subtilis)	57	38	1851
141	6	6395	7438	gi|995560	unknown (Schizosaccharomyces pombe)	57	41	1044
144	3	3231	2785	gnl|PID|d100139	ORF (Acetobacter pasteurianus)	57	42	447
155	4	5454	4564	gi|600431	glycosyl transerase (Erwinia amylovora)	57	34	891
159	9	4877	5854	gi|290509	o307 (Escherichia coli)	57	35	978
167	11	9710	9249	gnl|PID|d100139	ORF (Acetobacter pasteurianus)	57	42	462
171	6	4023	4436	gi|147402	mannose permease subunit III-Man (Escherichia coli)	57	29	414
178	4	2170	1076	gnl|PID|d102004	(AB001488) ATP-DEPENDENT RNA HELICASE DEAD HOMOLOG. (Bacillus subtilis)	57	39	1095
190	1	145	1455	gi|149420	export/processing protein (Lactococcus lactis)	57	30	1311
198	1	298	95	gi|522268	unidentified ORF22 (Bacteriophage bIL67)	57	36	204
203	2	3195	2110	gnl|PID|e283915	orf c01003 (Sulfolobus solfataricus)	57	41	1086
205	1	40	507	gi|1439527	EIIA-man (Lactobacillus curvatus)	57	28	468
214	7	4243	3797	gnl|PID|d102049	H. influenzae, ribosomal protein alanine acetyltransferase; P44305 (189) (Bacillus subtilis)	57	48	447
268	3	1767	1276	gi|43979	L.curvatus small cryptic plasmid gene for rep protein (Lactobacillus curvatus)	57	36	492
351	1	324	34	gnl|PID|e275871	T03F6.b (Caenorhabditis elegans)	57	31	291
386	1	226	2	gi|160671	S antigen precursor (Plasmodium falciparum)	57	45	225
5	5	10486	8777	gi|405857	yehU (Escherichia coli)	56	33	1710
8	5	3674	3910	gi|467199	pksC; L518_F1_2 (Mycobacterium leprae)	56	39	237
10	3	3442	1874	gnl|PID|d101907	sodium-coupled permease (Synechocystis sp.)	56	36	1569
21	1	1880	333	gi|2313949	(AE000593) osmoprotection protein (proWX) (Helicobacter pylori)	56	33	1548
22	29	21968	22456	gnl|PID|d102001	(AB001488) PROBABLE ACETYLTRANSFERASE. (Bacillus subtilis)	56	37	489
27	1	1361	3	gi|215132	ea59 (525) (Bacteriophage lambda)	56	30	1359
28	9	4667	4278	gi|1592090	DNA repair protein RAD2 (Methanococcus jannaschii)	56	29	390
33	1	3	386	gnl|PID|d100139	ORF (Acetobacter pasteurianus)	56	41	384

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
36	7	5122	5397	pir|PQ0053|PQ00	hypothetical protein (proC 3' region) - Pseudomonas aeruginosa (strain PAO) (fragment)	56	28	276
40	4	3137	4318	gi|1800301	macrolide-efflux determinant (Streptococcus pneumoniae)	56	27	1182
40	16	12511	13191	gnl|PID|e217602	PlnU (Lactobacillus plantarum)	56	38	681
48	17	13775	13023	gi|143729	transcription activator (Bacillus subtilis)	56	35	753
75	4	1674	2594	gnl|PID|d102036	membrane protein (Bacillus stearothermophilus)	56	25	921
85	3	1842	1459	gnl|PID|d100139	ORF (Acetobacter pasteurianus)	56	41	384
89	7	5815	4940	gi|853777	product similar to E coli PRFA2 protein (Bacillus subtilis)	56	42	876
105	2	1360	2718	gnl|PID|d101913	hypothetical protein (Synechocystis sp.)	56	37	1359
112	3	2151	3194	gi|537201	ORF_o345 (Escherichia coli)	56	31	1044
113	4	2754	2963	gnl|PID|d100340	ORF (Plum pox virus)	56	28	210
122	3	1203	2054	gi|1649035	high-affinity periplasmic glutamine binding protein (Salmonella typhimurium)	56	30	852
124	8	3939	3694	gnl|PID|e248893	unknown (Mycobacterium tuberculosis)	56	27	246
125	4	4403	4107	gnl|PID|d100247	human non-muscle myosin heavy chain (Homo sapiens)	56	32	297
127	11	6608	6405	gi|2182397	(AE000073) YdfN (Rhizobium sp. NGR234)	56	35	204
134	5	4769	3849	gnl|PID|d101870	hypothetical protein (Synechocystis sp.)	56	39	921
137	10	6814	7245	gi|1592011	sulfate permease (cysA) (Methanococcus jannaschii)	56	34	432
142	8	5019	4582	pir|A47071|A470	orf1 immediately 5' of nifS - Bacillus subtilis	56	29	438
146	8	4676	3660	gnl|PID|d101911	hypothetical protein (Synechocystis sp.)	56	32	1017
148	3	1906	2739	gnl|PID|d101099	phosphate transport system permease protein PstA (Synechocystis sp.)	56	36	834
150	4	4449	2743	gnl|PID|e304628	probably site-specific recombinase of the resolvase family of enzymes (Bacteriophage TP21)	56	27	1707
172	1	2	208	gi|1787791	(AE000249) f317; This 317 aa orf is 27 pct identical (16 gaps) to 301 residues of an approx. 320 aa protein YXXC_BACSU SW: P39140 (Escherichia coli)	56	34	207
172	7	4979	5668	gi|396293	similar to Bacillus subtilis hypoth. 20 kDa protein, in tsr 3' region (Escherichia coli)	56	40	690
186	7	3732	3367	gi|1732200	PTS permease for mannose subunit IIPMan (Vibrio furnissii)	56	36	366
187	2	2402	819	pir|S57904|S579	virR49 protein - Streptococcus pyogenes (strain CS101, serotype M49)	56	35	1584

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match accession	match gene name	% sim	% ident	length (nt)
204	3	2772	2239	gi|606376	ORF_o162 (Escherichia coli)	56	35	534
206	2	3342	1633	gi|559861	clyM (Plasmid pADI)	56	38	1710
219	3	1689	1096	gi|1146197	putative (Bacillus subtilis)	56	27	594
230	2	409	1485	pir|C60328|C603	hypothetical protein 2 (sr 5' region) - Streptococcus mutans (strain OMZ175, serotype f)	56	40	1077
233	4	2930	3268	gi|1041785	rhoptry protein (Plasmodium yoelii)	56	24	339
273	2	1543	2724	gi|143089	lep protein (Bacillus subtilis)	56	32	1182
353	1	1	516	gnl|PID|e325000	hypothetical protein (Bacillus subtilis)	56	41	516
359	1	87	641	gi|1786952	(AE000176) o877; 100 pct identical to the first 86 residues of the 100 aa hypothetical protein fragment YBGB_ECOLI SW: P54746 (Escherichia coli)	56	46	555
361	7	4482	4198	gi|1573353	outer membrane integrity protein (tolA) (Haemophilus influenzae)	56	38	285
376	1	2	508	gnl|PID|e325031	hypothetical protein (Bacillus subtilis)	56	33	507
18	1	836	177	gnl|PID|d100872	a negative regulator of pho regulon (Pseudomonas aeruginosa)	55	31	660
28	4	1824	1618	gnl|PID|e316518	STAT protein (Dictyostelium discoideum)	55	40	207
29	6	4496	5041	gi|1088261	unknown protein (Anabaena sp.)	55	31	546
38	16	9695	10702	gi|580905	B.subtilis genes rpmH, rnpA, 50kd, gidA and gidB (Bacillus subtilis)	55	31	1008
49	5	5727	6182	gi|1786951	(AE000176) heat-responsive regulatory protein (Escherichia coli)	55	29	456
51	4	2381	3241	gnl|PID|d101293	YbbA (Bacillus subtilis)	55	42	861
52	9	9640	10866	gi|153016	ORF 419 protein (Staphylococcus aureus)	55	23	1227
53	4	1813	1349	gi|896042	OspF (Borrelia burgdorferi)	55	30	465
60	5	4794	5756	gi|1499876	magnesium and cobalt transport protein (Methanococcus jannaschii)	55	38	963
71	9	14176	15408	gi|1857120	glycosyl transferase (Neisseria meningitidis)	55	41	1233
75	6	3189	4229	gnl|PID|e209890	NAD alcohol dehydrogenase (Bacillus subtilis)	55	44	1041
108	10	10488	9820	gnl|PID|e324997	hypothetical protein (Bacillus subtilis)	55	36	669
113	12	12273	13037	gnl|PID|e311496	unknown (Bacillus subtilis)	55	34	765
113	11	13007	13945	gi|157342	1-phosphofructokinase (fruK) (Haemophilus influenzae)	55	39	939
126	5	6764	5907	gi|1790131	(AE000446) hypothetical 29.7 kD protein in ibpA-gyrB intergenic region (Escherichia coli)	55	37	858

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
129	3	2719	902	gnl|PID|d101425	Pz-peptidase (Bacillus licheniformis)	55	35	1818
138	3	2593	1610	gi|142833	ORF2 (Bacillus subtilis)	55	37	984
140	6	6916	5633	gnl|PID|d100964	homologue of hypothetical protein in a rapamycin synthesis gene cluster of Streptomyces hygroscopicus (Bacillus subtilis)	55	26	1284
147	3	3854	2136	gi|472330	dihydrolipoamide dehydrogenase (Clostridium magnum)	55	39	1719
147	10	10204	8921	gnl|PID|e73078	dihydroorotase (Lactobacillus leichmannii)	55	38	1284
148	5	3430	4119	gi|290572	peripheral membrane protein U (Escherichia coli)	55	29	690
148	6	4171	4650	gi|695769	transposase (Xanthobacter autotrophicus)	55	37	480
149	14	12564	11650	gnl|PID|d101329	YqjG (Bacillus subtilis)	55	32	915
156	3	1113	550	gi|2314496	(AE000634) conserved hypothetical integral membrane protein (Helicobacter pylori)	55	34	564
159	10	6625	5897	gi|290533	similar to E. coli ORF adjacent to suc operon; similar to gntR class of regulatory proteins (Escherichia coli)	55	29	729
164	3	1784	2332	gnl|PID|e255118	hypothetical protein (Bacillus subtilis)	55	37	549
164	5	2772	3521	gi|40348	put. resolvase Tnp I (AA 1 - 284) (Bacillus thuringiensis)	55	35	750
164	11	7428	7216	gnl|PID|e249407	unknown (Mycobacterium tuberculosis)	55	38	213
167	5	3860	3345	gi|535052	involved in protein secretion (Bacillus subtilis)	55	28	516
186	5	2880	2563	gi|606080	ORF_o290; Geneplot suggests frameshift linking to o267, not found (Escherichia coli)	55	35	318
189	8	4311	5396	gnl|PID|e183450	hypothetical EcsB protein (Bacillus subtilis)	55	32	1086
192	5	3270	3079	gi|1196504	vitellogenin convertase (Aedes aegypti)	55	38	192
195	2	2454	1384	gi|1574693	transferase, peptidoglycan synthesis (murG) (Haemophilus influenzae)	55	33	1071
198	4	3013	2471	gnl|PID|e313074	hypothetical protein (Bacillus subtilis)	55	29	543
214	1	373	744	gnl|PID|d101741	transposase (Synechocystis sp.)	55	33	372
219	2	1115	456	gi|288301	ORF2 gene product (Bacillus megaterium)	55	30	660
263	7	3742	3443	gi|18137	cgcr-4 product (Chlamydomonas reinhardtii)	55	48	300
285	1	2	829	gnl|PID|d100974	unknown (Bacillus subtilis)	55	40	828
286	1	650	249	gi|396844	ORF (18 kDa) (Vibrio cholerae)	55	31	402
297	2	1229	1696	gi|150848	prtC (Porphyromonas gingivalis)	55	39	468

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
309	2	218	982	|gi|1574491	|hypothetical |Haemophilus influenzae|	55	35	765
328	2	646	224	|gi|571500	|prohibitin |Saccharomyces cerevisiae|	55	27	423
330	1	1340	474	|gi|396397	|soxS |Escherichia coli|	55	29	867
364	3	2538	1546	|gi|393394	|Tb-291 membrane associated protein |Trypanosoma brucei subgroup|	55	36	993
368	3	941	105	|gi|160671	|S antigen precursor |Plasmodium falciparum|	55	40	837
3	5	4604	3624	|gi|2293176	|(AF008220) signal transduction protein kinase |Bacillus subtilis|	54	26	981
9	11	7746	7246	|gi|1146245	|putative |Bacillus subtilis|	54	38	501
18	24	16213	17937	|gi|1480429	|putative transcriptional regulator |Bacillus stearothermophilus|	54	27	1725
40	8	5076	4882	|gi|39989	|methionyl-tRNA synthetase |Bacillus stearothermophilus|	54	35	195
43	4	3980	2367	|gnl|PID|e148611	|ABC transporter |Lactobacillus helveticus|	54	25	1614
52	10	10844	12103	|gi|1762962	|FemA |Staphylococcus simulans|	54	29	1260
57	1	3	512	|gi|558177	|endo-1,4-beta-xylanase |Cellulomonas fimi|	54	36	510
58	3	4749	4246	|gnl|PID|d101237	|hypothetical |Bacillus subtilis|	54	29	504
71	7	10684	11703	|gi|510255	|orf3 |Escherichia coli|	54	31	1020
71	20	27546	27737	|gi|202543	|serotonin receptor |Rattus norvegicus|	54	31	192
72	2	844	1098	|gi|148613	|srnB gene product |Plasmid F|	54	37	255
72	7	7438	6695	|gi|1196496	|recombinase |Moraxella bovis|	54	38	744
74	10	14043	13465	|gi|1200342	|ORF 3 gene product |Bradyrhizobium japonicum|	54	32	579
74	12	16483	15995	|gi|2317798	|maturase-related protein |Pseudomonas alcaligenes|	54	30	489
86	3	2877	2155	|gi|46988	|orf9.6 possibly encodes the O unit polymerase |Salmonella enterica|	54	34	723
89	5	4433	3921	|gi|147211	|phnO protein |Escherichia coli|	54	41	513
90	1	3	464	|gi|2317798	|maturase-related protein |Pseudomonas alcaligenes|	54	30	462
96	10	8058	8510	|gnl|PID|d102015	|(AB001488) SIMILAR TO SALMONELLA TYPHIMURIUM SLYY GENE REQUIRED FOR SURVIVAL IN MACROPHAGE. |Bacillus subtilis|	54	32	453
97	6	4662	3604	|gi|1591394	|transketolase'' |Methanococcus jannaschii|	54	30	1059
106	11	10406	12010	|gi|606286	|ORF_o63? |Escherichia coli|	54	32	1605
147	8	8663	7404	|gnl|PID|d101615	|ORF_ID:o31987; similar to |SwissProt Accession Number P37340| |Escherichia coli|	54	35	1260

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
171	4	2477	3223	gi|1439528	EIIC-man (Lactobacillus curvatus)	54	36	747
174	2	2068	1787	gnl|PID|d100518	motor protein (Homo sapiens)	54	35	282
188	1	526	1188	gnl|PID|e250352	unknown (Mycobacterium tuberculosis)	54	31	663
198	5	3582	2884	gnl|PID|e313074	hypothetical protein (Bacillus subtilis)	54	33	699
207	1	1	1641	gnl|PID|d101813	hypothetical protein (Synechocystis sp.)	54	24	1641
210	1	2	655	gi|2293206	(AF008220) YtmP (Bacillus subtilis)	54	29	654
225	2	966	2357	gnl|PID|e330194	R11H6.1 (Caenorhabditis elegans)	54	39	1392
241	1	1681	347	gnl|PID|d101813	hypothetical protein (Synechocystis sp.)	54	26	1335
263	2	907	1395	gnl|PID|d101886	transposase (Synechocystis sp.)	54	30	489
263	6	3450	2977	gi|160671	S antigen precursor (Plasmodium falciparum)	54	47	474
277	3	2517	1363	gi|1196926	unknown protein (Streptococcus mutans)	54	30	1155
307	1	828	4	gi|2293198	(AF008220) YtgP (Bacillus subtilis)	54	28	825
325	1	19	768	gi|2182507	(AE000083) Y4IH (Rhizobium sp. NGR234)	54	37	750
332	2	898	590	gi|1591815	ADP-ribosylglycohydrolase (draG) (Methanococcus jannaschii)	54	32	309
385	4	240	479	gi|530878	amino acid feature: N-glycosylation sites, aa 41 .. 43, 46 .. 48, 51 .. 53, 72 .. 74, 107 .. 109, 128 .. 130, 132 .. 134, 158 .. 160, 163 .. 165; amino acid feature: Rod protein domain, aa 169 .. 340; amino acid feature: globular protein domai	54	49	240
7	25	19702	19493	gnl|PID|e255111	hypothetical protein (Bacillus subtilis)	53	32	210
23	3	2497	2033	gnl|PID|d102015	(AB001488) SIMILAR TO SALMONELLA TYPHIMURIUM SLYY GENE REQUIRED FOR SURVIVAL IN MACROPHAGE. (Bacillus subtilis)	53	25	465
29	11	9042	10121	gi|143331	alkaline phosphatase regulatory protein (Bacillus subtilis)	53	31	1080
33	3	1479	1009	pir|S10655|S106	hypothetical protein X - Pyrococcus woesei (fragment)	53	33	471
36	6	4583	5134	gnl|PID|e316029	unknown (Mycobacterium tuberculosis)	53	30	552
38	14	8521	8898	gi|580904	homologous to E coli rnpA (Bacillus subtilis)	53	30	378
52	7	7007	8686	gi|1377831	unknown (Bacillus subtilis)	53	29	1680
54	17	17555	19564	gi|666069	orf2 gene product (Lactobacillus leichmannii)	53	36	2010
56	1	1	681	gi|1592266	restriction modification system S subunit (Methanococcus jannaschii)	53	32	681

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
57	10	9431	8487	|gi|1788543	(AE000310) f351; Residues 1-121 are 100 pct identical to YOJL_ECOLI SW: P33944 (122 aa) and aa 152-351 are 100 pct identical to YOJK_ECOLI SW: P33943 (Escherichia coli)	53	31	945
61	1	429	4	|gnl|PID|e236467	B0024.12 (Caenorhabditis elegans)	53	33	426
71	1	5772	4	|gi|393394	Tb-29l membrane associated protein (Trypanosoma brucei subgroup)	53	33	5769
72	3	894	2840	|gi|2293178	(AF008220) YtsD (Bacillus subtilis)	53	27	1947
73	14	9793	9212	|gi|1778556	putative cobalamin synthesis protein (Escherichia coli)	53	32	582
88	7	5217	4342	|gi|2098719	putative fimbrial-associated protein (Actinomyces naeslundii)	53	30	876
93	5	2395	1688	|gi|563366	gluconate oxidoreductase (Gluconobacter oxydans)	53	33	708
96	9	6632	7762	|gi|517204	ORF1, putative 42 kDa protein (Streptococcus pyogenes)	53	42	1131
108	8	7629	8600	|gi|149581	maturation protein (Lactobacillus paracasei)	53	32	972
128	9	6412	6972	|gnl|PID|e317237	unknown (Mycobacterium tuberculosis)	53	36	561
128	12	8429	9253	|gi|311070	pentraxin fusion protein (Xenopus laevis)	53	31	825
148	1	3	950	|pir|A61607|A616	probable hemolysin precursor - Streptococcus agalactiae (strain 74-360)	53	36	948
163	2	2162	3022	|gi|1755150	nocturnin (Xenopus laevis)	53	30	861
171	3	2304	2624	|gi|1732200	PTS permease for mannose subunit (IPMan (Vibrio furnissii)	53	32	321
182	5	3785	3051	|gnl|PID|d100572	unknown (Bacillus subtilis)	53	35	735
209	1	2948	1935	|gi|1778505	ferric enterobactin transport protein (Escherichia coli)	53	28	1014
218	5	3884	2406	|gi|40162	murE gene product (Bacillus subtilis)	53	34	1479
250	3	473	790	|gnl|PID|e334776	YibH protein (Bacillus subtilis)	53	30	318
275	1	1	1611	|gnl|PID|d101314	YqeW (Bacillus subtilis)	53	35	1611
332	1	544	2	|gi|409286	bmrU (Bacillus subtilis)	53	31	543
2	2	2543	3445	|gnl|PID|e233879	hypothetical protein (Bacillus subtilis)	52	39	903
3	22	22402	23376	|gi|38969	lacF gene product (Agrobacterium radiobacter)	52	36	975
5	3	8094	2356	|gnl|PID|e324915	IgA1 protease (Streptococcus sanguis)	52	32	5739
22	26	19961	20212	|gi|152901	ORF 3 (Spirochaeta aurantia)	52	35	252
22	31	23140	24666	|gi|289262	comE ORF3 (Bacillus subtilis)	52	32	1527
27	6	5397	4801	|gi|39573	P20 (AA 1-178) (Bacillus licheniformis)	52	35	597

TABLE 2

S pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match accession	match gene name	% sim	% ident	length (nt)
35	10	8604	7357	gi|508241	putative O-antigen transporter (Escherichia coli)	52	27	1248
45	4	4801	3662	gnl|PID|d10224	(AB005554) homologs are found in E. coli and H. influenzae; see SWISS_PROT ACC#: P42100 (Bacillus subtilis)	52	36	1140
48	18	14385	13726	gnl|PID|e205174	orf2 (Lactobacillus helveticus)	52	25	660
49	4	5321	5755	gi|2317740	(AF013987) nitrogen regulatory IIA protein (Vibrio cholerae)	52	19	435
54	4	2773	4668	gi|1500472	M. jannaschii predicted coding region MJ1577 (Methanococcus jannaschii)	52	36	1896
54	6	5250	4969	gi|218245	(AE000079) Y4IO (Rhizobium sp. NGR234)	52	40	282
66	6	8400	6955	gi|43140	TrkG protein (Escherichia coli)	52	30	1446
71	26	30659	31312	gnl|PID|e314993	unknown (Mycobacterium tuberculosis)	52	23	654
75	2	1673	1035	gnl|PID|d102271	(AB001683) FarA (Streptomyces sp.)	52	27	639
81	3	1439	2893	gnl|PID|e311458	rhamnulose kinase (Bacillus subtilis)	52	32	1455
81	8	4987	5781	gi|147403	mannose permease subunit II-P-Man (Escherichia coli)	52	37	795
83	21	20687	21853	gi|143365	phosphoribosyl aminoimidazole carboxylase II (PUR-K; ttg start codon) (Bacillus subtilis)	52	37	1167
86	6	5785	4592	gi|1276879	EpsF (Streptococcus thermophilus)	52	26	1194
86	20	19390	17861	gi|454844	ORF 3 (Schistosoma mansoni)	52	26	1530
96	13	10540	9659	gi|288299	ORF1 gene product (Bacillus megaterium)	52	33	882
111	1	2	2026	gi|148309	cytolysin B transport protein (Enterococcus faecalis)	52	27	2025
112	2	1457	2167	gi|471234	orf1 (Haemophilus influenzae)	52	33	711
118	3	2931	2365	bbs|151233	Mip=24 kda macrophage infectivity potentiator protein (Legionella pneumophila, Philadelphia-1, Peptide, 184 aa) (Legionella pneumophila)	52	33	567
122	9	5646	5951	gi|8214	myosin heavy chain (Drosophila melanogaster)	52	36	306
122	11	6159	6374	gi|434025	dihydrolipoamide acetyltransferase (Pelobacter carbinolicus)	52	52	216
134	6	4880	6313	gi|153733	M protein trans-acting positive regulator (Streptococcus pyogenes)	52	43	1434
135	3	1238	2716	gnl|PID|e245024	unknown (Mycobacterium tuberculosis)	52	35	1479
141	3	1681	2319	gnl|PID|d100573	unknown (Bacillus subtilis)	52	32	639
161	4	2562	5024	gi|1146243	22.4% identity with Escherichia coli DNA-damage inducible protein ...; putative (Bacillus subtilis)	52	36	2463
173	2	968	183	gi|1215693	putative orf; GT9_orf434 (Mycoplasma pneumoniae)	52	30	786

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
198	6	4400	3567	|gnl|PID|e313010	|hypothetical protein (Bacillus subtilis)	52	26	834
210	12	8844	9107	|gi|497647	|DNA gyrase subunit B (Mycoplasma genitalium)	52	38	264
214	10	5264	5431	|gi|550697	|envelope protein (Human immunodeficiency virus type 1)	52	36	168
225	1	15	884	|gi|1552773	|hypothetical (Escherichia coli)	52	34	870
230	1	39	362	|gnl|PID|d100582	|unknown (Bacillus subtilis)	52	28	324
287	1	871	2	|gnl|PID|e335028	|protease/peptidase (Mycobacterium leprae)	52	29	870
363	2	1305	4	|gi|393394	|Tb-291 membrane associated protein (Trypanosoma brucei subgroup)	52	32	1302
23	2	2048	1173	|gnl|PID|e254943	|unknown (Mycobacterium tuberculosis)	51	30	876
29	3	742	1521	|gi|929900	|5'-methylthioadenosine phosphorylase (Sulfolobus solfataricus)	51	31	780
45	1	410	1597	|gi|1877429	|integrase (Streptococcus pyogenes phage T12)	51	32	1188
48	26	19227	18946	|gi|2314455	|(AE000633) transcriptional regulator (tenA) (Helicobacter pylori)	51	33	282
73	5	4276	4016	|gi|474177	|alpha-D-1,4-glucosidase (Staphylococcus xylosus)	51	31	261
81	11	8935	12057	|gi|311070	|pentraxin fusion protein (Xenopus laevis)	51	31	3123
83	5	1195	1986	|gnl|PID|d101316	|YqfI (Bacillus subtilis)	51	33	792
98	10	7531	8538	|gi|41500	|ORF_3 (AA 1-352); 38 kD (put. ftsX) (Escherichia coli)	51	28	1008
113	6	3908	5173	|gi|466882	|pps1; B1496_C2_189 (Mycobacterium leprae)	51	27	1266
124	1	326	57	|gi|2191168	|(AF007270) contains similarity to myosin heavy chain (Arabidopsis thaliana)	51	32	270
129	10	7286	6816	|gi|1046241	|orf14 (Bacteriophage HP1)	51	30	471
143	3	4963	3983	|gi|1354935	|probable copper-transporting atpase (Escherichia coli)	51	26	981
148	15	11359	10226	|gi|2293256	|(AF008220) putative hippurate hydrolase (Bacillus subtilis)	51	36	1134
149	8	6003	7313	|gi|1633572	|Herpesvirus saimiri ORF73 homolog (Kaposi's sarcoma-associated herpes-like virus)	51	21	1311
151	9	12092	11550	|gnl|PID|e281580	|hypothetical 40.7 kd protein (Bacillus subtilis)	51	34	543
159	6	2555	3208	|gi|146944	|CMP-N-acetylneuraminic acid synthetase (Escherichia coli)	51	36	654
174	1	1797	4	|gi|1773166	|probable copper-transporting atpase (Escherichia coli)	51	28	1794
265	4	2231	1773	|gnl|PID|e256400	|anti-P.falciparum antigenic polypeptide (Saimiri sciureus)	51	18	459
277	2	643	1311	|pir|S32915|S329	|pilD protein - Neisseria gonorrhoeae	51	33	669

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
350	1	890	3	|gi|290509	|o307 (Escherichia coli)	51	30	888
363	4	1228	4485	|gi|1707247	|partial COS (Caenorhabditis elegans)	51	23	3258
367	1	1701	4	|gi|393394	|Tb-291 membrane associated protein (Trypanosoma brucei subgroup)	51	32	1698
15	5	5174	4497	|gnl|PID|e58151	|F) (Bacillus subtilis)	50	38	678
16	4	2220	2582	|gnl|PID|e325010	|hypothetical protein (Bacillus subtilis)	50	29	363
19	5	2591	4159	|gi|1552733	|similar to voltage-gated chloride channel protein (Escherichia coli)	50	30	1569
25	4	2701	1997	|gi|887849	|ORF_f219 (Escherichia coli)	50	27	705
35	1	211	617	|gnl|PID|e236697	|unknown (Saccharomyces cerevisiae)	50	33	207
39	4	3416	5152	|gnl|PID|d100974	|unknown (Bacillus subtilis)	50	27	1737
51	7	4000	5181	|gi|1592027	|carbamoyl-phosphate synthase, pyrimidine-specific, large subunit (Methanococcus jannaschii)	50	27	1182
51	9	7179	8303	|gi|1591847	|type I restriction-modification enzyme, S subunit (Methanococcus jannaschii)	50	28	1125
52	8	8740	9534	|gi|144297	|acetyl esterase (XynC) (Caldocellum saccharolyticum)	50	34	795
52	16	16591	15770	|gi|2108229	|basic surface protein (Lactobacillus fermentum)	50	34	822
57	7	6031	6336	|gi|2275264	|60S ribosomal protein L7B (Schizosaccharomyces pombe)	50	40	306
71	23	29348	28383	|gnl|PID|d101328	|YqjA (Bacillus subtilis)	50	30	966
86	12	11155	10769	|gnl|PID|e324964	|hypothetical protein (Bacillus subtilis)	50	24	387
93	2	1205	330	|gi|1066016	|similar to Escherichia coli pyruvate, water dikinase, Swiss-Prot Accession Number P23538 (Pyrococcus furiosus)	50	24	876
96	5	1673	2959	|gnl|PID|e322433	|gamma-glutamylcysteine synthetase (Brassica juncea)	50	29	1287
98	2	218	1171	|gi|151110	|leucine-, isoleucine-, and valine-binding protein (Pseudomonas aeruginosa)	50	30	954
103	4	3303	2785	|gi|154330	|O-antigen ligase (Salmonella typhimurium)	50	31	519
115	5	6480	5980	|gi|895747	|putative cel operon regulator (Bacillus subtilis)	50	26	501
129	11	7559	7305	|gi|1216475	|skeletal muscle ryanodine receptor (Homo sapiens)	50	32	255
129	13	8192	7965	|gi|152271	|319-kDA protein (Rhizobium meliloti)	50	30	228
151	5	7634	6819	|gi|40348	|put. resolvase Tnp I (AA 1 - 284) (Bacillus thuringiensis)	50	35	816
153	1	1	597	|gnl|PID|d102015	|(AB0014881 SIMILAR TO NITROREDUCTASE. (Bacillus subtilis)	50	29	597

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
155	5	5986	5432	gi|1276880	EpsG (Streptococcus thermophilus)	50	28	555
160	9	7390	6323	gi|1786983	(AE000179) o331; 92 pct identical to the 333 aa hypothetical protein YBHE_ECOLI SW: P52697; 26 pct identical (7 gaps) to 167 residues of the 373 aa protein HLE_TRICU SW: P46057; SW: P52697 (Escherichia coli)	50	30	1068
163	6	7396	8091	gnl|PID|d101313	YqeN (Bacillus subtilis)	50	22	696
167	6	5232	3940	gi|413926	ipa-2r gene product (Bacillus subtilis)	50	27	1293
169	2	807	130	gnl|PID|e304540	endolysin (Bacteriophage Bastille)	50	35	678
171	5	3160	4025	gi|606080	ORF_o290; Geneplot suggests frameshift linking to o267, not found (Escherichia coli)	50	27	858
210	11	8151	8414	gi|330038	HRV 2 polyprotein (Human rhinovirus)	50	25	264
364	1	1538	135	gi|393396	Tb-292 membrane associated protein (Trypanosoma brucei subgroup)	50	31	1404
10	7	5911	5090	gi|144859	ORF B (Clostridium perfringens)	49	24	822
26	5	10754	9768	gi|142440	ATP-dependent nuclease (Bacillus subtilis)	49	31	987
66	7	9777	8398	gi|414170	trkA gene product (Methanosarcina mazeii)	49	26	1380
77	6	5364	4648	gnl|PID|e285322	RecX protein (Mycobacterium smegmatis)	49	28	717
82	11	12689	13249	gnl|PID|e255091	hypothetical protein (Bacillus subtilis)	49	20	561
93	9	4866	4531	gi|40067	X gene product (Bacillus sphaericus)	49	26	336
112	5	4019	4948	gi|1574380	lic-1 operon protein (licB) (Haemophilus influenzae)	49	27	930
129	7	6058	4949	gnl|PID|e267587	Unknown (Bacillus subtilis)	49	35	1110
135	5	3875	4438	gi|39573	P20 (AA 1-178) (Bacillus licheniformis)	49	25	564
154	2	1423	1953	gnl|PID|d101102	regulatory components of sensory transduction system (Synechocystis sp.)	49	29	531
156	5	2878	1637	gnl|PID|d101732	hypothetical protein (Synechocystis sp.)	49	25	1242
173	5	3500	2940	gi|490324	(LORF X gene product (unidentified)	49	30	561
182	1	1057	2	gi|331002	first methionine codon in the ECLF1 ORF (Saimiriine herpesvirus 2)	49	25	1056
192	6	5352	3667	gi|2394472	(AF024499) contains similarity to homeobox domains (Caenorhabditis elegans)	49	23	1686
253	4	1129	1350	gi|531116	SIN4 protein (Saccharomyces cerevisiae)	49	23	222
277	1	600	136	gi|396844	ORF (18 kDa) (Vibrio cholerae)	49	32	465
327	1	1435	887	gi|733524	phosphatidylinositol-4,5-diphosphate 3-kinase (Dictyostelium discoideum)	49	24	549

TABLE 2

S pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
365	3	1436	132	|gi|393394	|Tb-291 membrane associated protein (Trypanosoma brucei subgroup)	49	31	1305
33	7	4461	3277	|gi|145644	|codes for a protein of unknown function (Escherichia coli)	48	26	1185
40	2	652	1776	|gnl|PID|e290649	|ornithine decarboxylase (Nicotiana tabacum)	48	29	1125
67	4	3377	2384	|gi|1772652	|2-keto-3-deoxygluconate kinase (Haloferax alicantei)	48	30	1008
74	2	4269	3871	|gi|2182670	|(AE000101) Y4vJ (Rhizobium sp. NGR234)	48	27	399
81	2	1326	541	|gi|153672	|lactose repressor (Streptococcus mutans)	48	33	786
81	4	2981	3646	|gi|146042	|fuculose-1-phosphate aldolase (fucA) (Escherichia coli)	48	30	666
97	1	602	51	|gi|153794	|rgg (Streptococcus gordonii)	48	29	552
110	1	1	3132	|gi|1381114	|prtB gene product (Lactobacillus delbrueckii)	48	23	3132
131	5	2914	2147	|gnl|PID|e183811	|Acyl-ACP thioesterase (Brassica napus)	48	27	768
133	4	3494	2628	|gnl|PID|e261988	|putative ORF (Bacillus subtilis)	48	27	867
139	6	4231	4599	|gi|1049388	|ZK470.1 gene product (Caenorhabditis elegans)	48	23	369
139	8	5036	5665	|gi|1022725	|unknown (Staphylococcus haemolyticus)	48	29	630
140	12	11936	11007	|gnl|PID|d102049	|H. influenzae, ribosomal protein alanine acetyltransferase; P44305 (189) (Bacillus subtilis)	48	27	930
146	9	5670	4654	|gi|1591731	|melvalonate kinase (Methanococcus jannaschii)	48	24	1017
161	3	1280	2374	|gnl|PID|d101578	|Collagenase precursor (EC 3.4.-.-). (Escherichia coli)	48	24	1095
172	11	10581	11048	|gnl|PID|d101132	|hypothetical protein (Synechocystis sp.)	48	27	468
182	4	2930	2586	|gi|40067	|X gene product (Bacillus sphaericus)	48	37	345
210	15	10786	11196	|sp|P13940|LE29_	|LATE EMBRYOGENESIS ABUNDANT PROTEIN D-29 (LEA D-29).	48	30	411
214	12	6231	6482	|gi|40389	|non-toxic components (Clostridium botulinum)	48	26	252
221	1	704	3	|gi|1573364	|H. influenzae predicted coding region HI0392 (Haemophilus influenzae)	48	27	702
227	2	647	3928	|gi|1673693	|(AE000005) Mycoplasma pneumoniae, C09_orf718 Protein (Mycoplasma pneumoniae)	48	30	3282
253	2	480	758	|gnl|PID|e236697	|unknown (Saccharomyces cerevisiae)	48	31	279
363	3	1874	1122	|gi|18137	|cgcr-4 product (Chlamydomonas reinhardtii)	48	40	753
389	1	505	2	|gi|18137	|cgcr-4 product (Chlamydomonas reinhardtii)	48	38	504
3	21	20879	22258	|gnl|PID|e264778	|putative maltose-binding pootein (Streptomyces coelicolor)	47	33	1380

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins sImilar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
6	4	4089	4658	gi|39573	P20 (AA 1-178) [Bacillus licheniformis]	47	23	570
15	3	3736	1760	gnl|PID|d100572	unknown [Bacillus subtilis]	47	25	1977
35	15	14516	13263	gi|1773351	Cap5L [Staphylococcus aureus]	47	20	1254
51	6	3547	4002	pir|A37024|A370	32K antigen precursor - Mycobacterium tuberculosis	47	38	456
55	8	10154	9273	gi|39848	U3 [Bacillus subtilis]	47	26	882
92	4	1753	3276	gnl|PID|e280611	PCPC [Streptococcus pneumoniae]	47	35	1524
127	9	5589	5386	gi|1786458	(AE000134) f120; This 120 aa orf is 76 pct identical (0 gaps) to 42 residues of an approx. 48 aa protein Y127_HAEIN SW: P43949 [Escherichia coli]	47	32	204
110	2	1232	1759	gnl|PID|e266555	unknown [Mycobacterium tuberculosis]	47	23	528
140	4	4951	3542	gnl|PID|d100964	homologue of hypothetical protein in a rapamycin synthesis gene cluster of Streptomyces hygroscopicus [Bacillus subtilis]	47	24	1410
151	4	6814	6200	gi|1522674	M. jannaschii predicted coding region MJECL41 [Methanococcus jannaschii]	47	27	615
157	3	803	1174	gnl|PID|d101320	Yqg2 [Bacillus subtilis]	47	25	372
178	5	3267	2155	gi|2367190	(AE000390) o334; sequence change joins ORFs ygjR & ygjS from earlier version (YGJR_ECOLI SW: P42599 and YGJS_ECOLI SW: P42600) [Escherichia coli]	47	30	1113
273	1	2	1549	gnl|PID|e254973	autolysin sensor kinase [Bacillus subtilis]	47	32	1548
300	2	880	644	gi|1835755	zinc finger protein Png-1 [Mus musculus]	47	22	237
54	14	14182	12638	pir|S43609|S436	rofA protein - Streptococcus pyogenes	46	24	1545
88	1	2	1018	gnl|PID|e223891	xylose repressor [Anaerocellum thermophilum]	46	27	1017
96	7	4553	5860	gnl|PID|d101652	ORF_ID:o34785; similar to [SwissProt Accession Number P45272] [Escherichia coli]	46	23	1308
112	1	1127	3	gi|2209215	(AF004325) putative oligosaccharide repeat unit transporter [Streptococcus pneumoniae]	46	24	1125
122	13	7308	7982	gi|1054776	hr44 gene product [Homo sapiens]	46	34	675
127	14	9198	8125	gi|1469286	afuA gene product [Actinobacillus pleuropneumoniae]	46	28	1074
132	4	7093	6197	gi|153794	rgg [Streptococcus gordonii]	46	26	897
140	8	8220	7723	gi|1235795	pullulanase [Thermosnaerobacterium thermosulfurigenes]	46	21	498
140	9	9205	8315	gi|407878	leucine rich protein [Streptococcus equisimilis]	46	27	891

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match accession	match gene name	% sim	% ident	length (nt)
162	1	1	1125	gi|1143209	ORF7; Method: conceptual translation supplied by author (Shigella sonnei)	46	25	1125
199	1	1	585	gi|1947171	(AF000299) No definition line found (Caenorhabditis elegans)	46	28	585
223	3	1971	1477	sp|P02562|MYSS_	MYOSIN HEAVY CHAIN, SKELETAL MUSCLE (FRAGMENTS).	46	27	495
232	2	760	1608	gi|1016112	ycf38 gene product (Cyanophora paradoxa)	46	28	849
292	1	687	220	gi|1673744	(AE000011) Mycoplasma pneumoniae, cytidine deaminase; similar to GenBank Accession Number C53312, from M. pirum (Mycoplasma pneumoniae)	46	29	468
30	8	5843	6472	gi|1788049	(AE000270) o235; This 235 aa orf is 29 pct identical (10 gaps) to 198 residues of an approx. 216 aa protein YTXB_BACSU SW: P06568 (Escherichia coli)	45	24	630
48	6	3461	3868	gi|722339	unknown (Acetobacter xylinum)	45	29	408
60	1	307	2	gi|1699079	coded for by C. elegans cDNA yk41h4.3; coded for by C. elegans cDNA yk148g10.5; coded for by C. elegans cDNA yk152g5.5; coded for by C. elegans cDNA yk59a10.5; coded for by C. elegans cDNA yk41h4.5; coded for by C. elegans cDNA cm20g10; coded	45	36	306
72	16	14371	14874	gi|1321900	NADH dehydrogenase (ubiquinone) (Artemia franciscana)	45	25	504
99	7	9158	7941	gi|152192	mutation causes a succinoglucan-minus phenotype; ExoQ is atransmembrane protein; third gene of the exoYFQ operon;; putative (Rhizobium meliloti)	45	28	1218
127	12	7046	6606	bbs|153689	HitB=iron utilization protein (Haemophilus influenzae, type b, DL42, NTHI TN106, Peptide, 506 aa) (Haemophilus influenzae)	45	24	441
137	5	1561	2619	gi|472921	v-type Na-ATPase (Enterococcus hirae)	45	31	1059
209	1	774	364	gi|304141	restriction endonuclease beta subunit (Bacillus coagulans)	45	28	411
314	1	604	2	gi|1480457	latex allergen (Hevea brasiliensis)	45	31	603
20	18	19782	20288	gi|433942	ORF (Lactococcus lactis)	44	26	507
87	8	7030	6452	gi|537207	ORF_f277 (Escherichia coli)	44	26	579
166	5	4909	4037	gnl|PID|e308082	membrane transport protein (Bacillus subtilis)	44	25	873
247	1	818	75	gnl|PID|d100718	ORF1 (Bacillus sp.)	44	20	744
32	3	1885	3876	gi|2351768	PspA (Streptococcus pneumoniae)	43	24	1992
36	17	15467	18256	gi|1045739	M. genitalium predicted coding region MG064 (Mycoplasma genitalium)	43	26	2790
54	15	14656	17343	gi|520541	penicillin-binding proteins 1A and 1B (Bacillus subtilis)	43	27	2688
67	2	696	1352	gi|536934	yjcA gene product (Escherichia coli)	43	29	657
139	2	2416	338	gi|396400	similar to eukaryotic Na+/H+ exchangers (Escherichia coli)	43	24	2079

TABLE 2

S. pneumoniae - Putative coding regions of novel proteins similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)	match acession	match gene name	% sim	% ident	length (nt)
298	1	3	809	gi|413972	ipa-48r gene product (Bacillus subtilis)	43	24	807
387	1	47	427	gi|2315652	(AF016669) No definition line found (Caenorhabditis elegans)	43	30	381
185	4	4221	3127	gi|2182399	(AE000073) Y4fP (Rhizobium sp. NGR234)	41	25	1095
340	1	582	70	gnl|PID|e218681	CDP-diacylglycerol synthetase (Arabidopsis thaliana)	41	20	513
363	6	4205	1914	gi|1256742	R27-2 protein (Trypanosoma cruzi)	41	27	2292
368	2	2	943	gi|21783	LMW glutenin (AA 1-356) (Triticum aestivum)	41	34	942
155	3	4489	2861	gi|42023	member of ATP-dependent transport family, very similar to mdr proteins and hemolysin B, export protein (Escherichia coli)	40	18	1629
365	2	95	1438	gi|1633572	Herpesvirus saimiri ORF73 homolog (Kaposi's sarcoma-associated herpes-like virus)	40	21	1344
1	3	2979	3860	gnl|PID|d101908	hypothetical protein (Synechocystis sp.)	39	26	882
1	5	3814	4647	gnl|PID|d101961	hypothatical protein (Synechocystis sp.)	39	19	834
26	6	14035	10724	gi|142439	ATP-dependent nuclease (Bacillus subtilis)	38	20	3312
47	1	3	4916	gi|632549	NF-180 (Petromyzon marinus)	36	23	4914

TABLE 3

S. pneumoniae - Putative coding regions of novel proteins not similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
1	4	3428	3009
1	6	4611	4964
3	2	818	994
3	3	1182	1574
3	7	5382	6497
3	25	25046	25396
3	26	25625	26317
6	2	1519	1689
6	14	12875	12618
6	15	13215	12841
6	18	15977	15390
7	12	9955	9419
7	13	10161	9910
8	6	3915	4280
9	9	6024	5704
10	8	6909	6298
10	9	7136	6888
10	11	7968	7672
12	1	1140	4
12	3	1779	1456
14	2	1913	1434
16	1	1	243
16	5	5675	3087
17	1	324	34
17	3	1451	1050
17	9	4890	4465
20	14	14544	15893

TABLE 3

S. pneumoniae - Putative coding regions of novel proteins not similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
21	3	3359	2589
21	5	4802	4482
22	21	17099	17362
22	25	19467	19982
22	33	25540	25764
22	35	26388	26210
22	36	26382	27572
23	7	6655	6032
23	8	7132	6653
24	1	36	518
25	5	3009	2641
27	4	4819	4223
27	5	4789	4956
28	5	3017	1797
28	8	4272	3850
28	10	5028	4597
28	11	5746	5072
29	7	5596	4919
29	8	5039	5518
29	9	5595	8207
30	9	6511	6263
31	6	2664	2344
32	5	5203	5538
33	8	5327	4668
34	10	8024	7740
34	12	9360	8641
34	13	9667	9377

TABLE 3

S. pneumoniae - Putative coding regions of novel proteins not similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
34	18	13104	11902
35	11	9688	8588
35	12	11073	9670
36	2	334	1041
36	12	11120	10893
36	13	10993	11388
36	15	12172	14595
38	7	4269	4577
38	8	4480	5001
38	10	5517	5711
38	17	10732	11376
40	3	1728	3143
43	1	172	5
43	7	8884	8732
43	8	9568	9071
44	4	4831	6831
45	3	3204	3665
46	6	3875	3468
46	7	6074	7081
48	5	3196	3582
48	8	4579	4229
48	11	9323	8922
48	16	13042	12494
48	20	16342	15764
48	24	17971	18351
48	30	21979	21776
49	1	209	3

TABLE 3

S. pneumoniae - Putative coding regions of novel proteins not similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
50	4	3307	2672
51	5	3239	3598
52	11	12146	12883
54	7	5588	5187
54	8	6013	5659
54	9	6004	6210
54	16	17685	17506
55	9	10515	10123
55	12	11947	12141
56	3	935	1387
56	4	1496	1939
57	3	1624	2130
57	4	2100	2501
58	6	7541	7335
59	1	2	430
59	4	2416	2736
59	5	2734	3063
59	8	4743	5549
59	9	5459	5929
60	6	5741	6451
61	3	2395	1772
61	5	3316	3176
64	1	2722	2
66	2	1180	3147
66	8	9082	9495
67	3	1343	1182
69	2	1165	980

TABLE 3

S. pneumoniae - Putative coding regions of novel proteins not similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
70	5	4059	3922
70	6	4215	4057
70	9	5268	5504
71	15	20351	21901
71	16	21859	22338
71	19	26204	27556
72	9	8458	8081
73	4	3815	4216
73	6	4214	4582
73	7	4369	4773
73	10	7183	6428
73	15	9462	9668
76	1	524	195
76	2	867	535
76	11	8602	9210
80	6	7924	8109
81	1	244	2
81	10	6631	8931
83	4	1872	1150
83	17	16810	16460
84	3	4464	2929
86	2	2147	1092
86	4	3606	2875
86	19	16767	17114
87	5	5326	5000
87	7	6459	6001
87	9	7224	7006

TABLE 3

S. pneumoniae - Putative coding regions of novel proteins not similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
87	18	17930	17670
87	19	18275	17928
88	2	1619	1840
88	4	2711	2878
88	9	6252	6016
89	3	2634	1621
89	9	7371	6868
90	2	899	2395
90	3	1143	952
91	3	2959	3161
91	4	3170	3691
91	6	4253	4573
93	1	391	2
93	6	2648	2379
93	8	4533	3712
96	1	3	182
96	2	904	632
96	3	1407	1147
96	4	1250	1420
97	9	7043	6753
99	15	18522	18692
99	17	19717	19541
100	2	4094	1980
103	1	48	299
103	6	4924	4373
104	5	6142	6735
105	7	6098	6517

TABLE 3

S. pneumoniae - Putative coding regions of novel proteins not similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
106	1	1	363
106	10	9832	10212
108	1	2	268
111	3	3417	3788
111	4	3809	4606
115	10	10854	10438
116	3	2873	2121
118	2	2274	1357
122	4	2698	2333
122	10	5858	6199
122	12	6301	7416
124	2	346	690
128	4	2544	3368
129	1	689	102
129	2	1011	724
129	8	6454	6056
129	9	6540	6277
129	12	7809	7621
131	3	1433	756
131	10	5972	5673
134	11	11838	11209
135	2	625	1140
136	4	2913	3830
137	2	325	134
139	12	14027	14521
139	13	14840	14532
139	14	15363	14875

TABLE 3

S. pneumoniae - Putative coding regions of novel proteins not similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
140	20	19822	20838
142	1	1	285
146	3	760	479
146	6	1149	778
146	7	3604	2885
146	13	8223	9401
146	14	9399	10676
146	15	10052	9750
147	7	7488	7276
147	9	8913	8647
148	7	5298	4765
149	1	2	1936
149	3	2557	2880
149	9	6258	6070
150	2	1355	579
150	3	2556	1909
153	3	2061	2642
154	3	1953	1741
155	2	2181	1411
156	8	4550	4311
157	1	37	294
159	2	631	780
159	4	1384	1722
159	7	3271	4017
161	2	1332	1018
165	3	5535	4945
166	6	5406	4972

TABLE 3

S. pneumoniae - Putative coding regions of novel proteins not similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
167	9	6075	6395
169	5	2828	3205
170	7	6485	6243
170	8	6964	6362
170	9	7303	6962
170	11	8790	7906
171	9	7150	7476
172	5	2298	1948
173	4	2913	2677
175	2	659	835
175	3	893	1789
176	2	1487	546
176	3	2200	1466
177	9	4686	4925
177	10	4923	5177
177	11	5111	5367
177	13	7396	8703
178	6	3452	3724
181	5	1853	2473
182	2	2112	1102
182	3	2617	2006
183	2	2126	2320
185	5	4683	4219
185	6	4846	4634
187	4	2940	3557
188	4	3686	4363
188	5	4183	4021

TABLE 3

S. pneumoniae - Putative coding regions of novel proteins not similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
188	6	5882	6493
189	5	3143	2844
189	9	5956	5564
191	1	618	4
191	11	10357	10001
192	3	2861	2268
192	4	3081	2878
192	7	6800	5331
193	3	997	839
194	4	2315	2127
195	5	6249	4543
195	6	6620	6231
196	2	1553	1849
197	1	1	861
198	9	6844	6644
200	5	5329	5769
200	6	5993	6595
204	5	3914	3276
205	2	447	1709
209	4	2038	2460
209	5	2458	2682
210	10	7370	8230
210	13	9029	10441
210	14	10439	10705
214	5	2581	2330
214	9	5065	5277
214	11	5996	5754

TABLE 3

S. pneumoniae - Putative coding regions of novel proteins not similar to known protpins

Contig ID	ORF ID	Start (nt)	Stop (nt)
217	2	541	194
218	2	914	1432
218	3	1430	1972
218	6	3639	3821
219	1	458	39
220	1	869	600
223	4	2617	1964
227	1	1	510
234	4	1539	1312
234	6	2116	1838
235	1	52	312
235	2	310	687
238	1	660	64
246	1	1	270
248	1	3	362
248	2	443	1222
254	3	2789	792
258	2	1179	1616
260	3	1770	2123
263	1	653	177
263	4	2244	1900
263	5	3569	2973
266	1	1	342
266	2	177	1022
270	2	1124	1681
272	1	857	186
275	2	1684	2295

TABLE 3

S. pneumoniae - Putative coding regions of novel proteins not similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
278	1	2	406
282	1	716	391
282	4	1463	1134
287	2	1119	826
288	1	540	4
289	1	684	4
291	5	1589	1858
293	2	2539	2925
294	1	21	608
296	2	494	700
296	3	670	843
302	1	261	530
309	3	559	350
310	2	249	1889
316	2	2087	1818
317	2	1048	584
318	2	313	777
319	3	477	133
327	2	912	607
331	1	1	549
333	1	2	535
333	2	465	82
333	3	127	342
341	1	1	705
345	2	895	701
346	2	750	199
349	1	1	198

TABLE 3

S. pneumoniae - Putative coding regions of novel proteins not similar to known proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
350	2	81	413
355	1	44	973
358	2	636	448
360	2	948	628
364	2	1639	1265
378	1	345	1004
379	2	683	510
381	1	109	693
385	1	150	4
385	2	269	30

(1) GENERAL INFORMATION:

(i) APPLICANT: Charles Kunsch
Gil H. Choi
Patrick S. Dillon
Craig A. Rosen
Steven C. Barash
Michael R. Fannon
Brian A. Dougherty

(ii) TITLE OF INVENTION: Streptococcus pneumoniae Polynucleotides and Sequences

(iii) NUMBER OF SEQUENCES: 391

(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: Human Genome Sciences, Inc.
(B) STREET: 9410 Key West Avenue
(C) CITY: Rockville
(D) STATE: Maryland
(E) COUNTRY: USA
(F) ZIP: 20850

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Diskette, 3.50 inch, 1.4Mb storage
(B) COMPUTER: HP Vectra 486/33
(C) OPERATING SYSTEM: MSDOS version 6.2
(D) SOFTWARE: ASCII Text

(vi) CURRENT APPLICATION DATA:

AGGATTTTCC TTCAAATTTG GAGGTTCAAG GTCCTGTAGA ATTTGCAGCAA TTAGGGCAAA 9360

CTTTTAATGA GATGTCCCAT GATTTGCAGG TAAGCTTTGA TTCCTTGGAA GAAAGCGAAC 9420

GAGAAAAGGG CTTGATGATT GCCCAGTTGT CGCATGATAT TAAGACTCCT ATCACTTCGA 9480

TCCAAGCGAC GGTAGAAGGG ATTTTGGATG GGATTATCAA GGAGTCGGAG CAAGCTCATT 9540

ATCTAGCAAC CATTGGACGC CAGACGGAGA GGCTCAATAA ACTGGTTGAG GAGTTGAATT 9600

TTTTGACCCT AAACACAGCT AGAAATCAGG TGGAAACTAC CAGTAAAGAC AGTATTTTTC 9660

TGGACAAGCT CTTAATTGAG TGCATGAGTG AATTTCAGTT TTTGATTGAG CAGGAGAGAA 9720

GAGATGTCCA CTTGCAGGTA ATCCCAGAGT CTGCCCGGAT TGAGGGAGAT TATGCTAAGC 9780

TTTCTCGTAT CTTGGTGAAT CTGGTCGATA ACGCTTTTAA ATATTCTGCT CCAGGAACCA 9840

AGCTGGAAGT GGTGGCTAAG CTGGAGAAGG ACCAGCTTTC AATCAGTGTG ACCGATGAAG 9900

GGCAGGGTAT TGCCCCAGAG GATTTGGAAA ATATTTTCAA ACGCCTTTAT CGTGTCGAAA 9960

CTTCGCGTAA CATGAAGACA GGTGGTCATG GATTAGGACT TGCGATTGCG CGTGAATTGG 10020

CCCATCAATT GGGTGGGGAA ATCACAGTCA GCAGCCAGTA CGGTCTAGGA AGTACCTTTA 10080

CCCTCGTTCT CAACCTCTCT GGTAGTGAAA ATAAAGCCTA AAACCCCTTT ACAAATCCAG 10140

CTATTCATGG TAGAATAGAT TTTGTGTGAA ATATCAGCAG GAAAGCATGA AGCTCGTCAA 10200

CAGGTGTCTT ATGACAAGTA ACCTTGGCTG TTTAGGCGAA GGGCATCTGC ACGG 10254

(2) INFORMATION FOR SEQ ID NO: 30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9769 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

CCGGCGACTA TCGATAACAC TTGACTTGGT AGCCCCACAT TTTGGACAAC GCATCCTTTC 60

CCTCCTTATC GTTTTCTTTT CATTATACCA TTTTTTAAGC GATTCCCAAA ACAATTCTTC 120

TTTTTGCTTG ACAAGTTTTT TGTTTTGTTG TATTATTTAA TTAAGACAAC AAGGTAAAAG 180

AAAGGAGACT AAGATGTCCT GGACATTTGA CAACAAAAAA CCCATCTATT TACAGATTAT 240

GGAGAAAATC AAGCTTCAGA TTGTTTCCCA TACACTGGAA CCCAATCAAC AACTTCCAAC 300

CGTGAGGAGC TAGCTAGCGA GGCTGGTGTC AATCCCAATA CCATCCAAAG AGCCTTATCA 360

GACCTTGAAC GAGAAGGATT TGTCTACAGC AAGCGAACAA CTGGACGATT TGTGACTAAG 420

GATAAGGAGC TAATCGCCCA GTCACGCAAA CAATTATCAG AAGAAGAATT GGAACACTTC 480

GTTTCCTCCA TGACCCATTT TGGCTATGAA AAAGAAGAAC TACCAGGCGT AGTCAGTGAT 540

TATATTAAAG GAGTTTAAGC CTATGTCATT ACTAGTATTT GAAAATGTAT CCAAATCATA 600

TGGAGCAACA CCAGCCCTTG AAAATGTTTC TCTTGACATT CCAGCTGGAA AAATTGTCGG 660

CCTTCTTGGG CCAAACGGCT CAGGAAAAAC AACCCTGATT AAACTAATTA ATGGCCTCTT 720

ACAACCAGAT CAAGGACGTG TCCTCATCAA CGACATGGAC CCAAGCCCAG CAACCAAGGC 780

CGTTGTAGCT TATTTGCCTG ATACGACCTA TCTCAATGAG CAAATGAAGG TCAAAGAAGC 840

CCTAACCTAC TTCAAGACCT TCTATAAAGA TTGTCAGATC TTGAACGCGC CCATCATCTA 900

CTTGCAGACC TGGGCATTGA TGAAAATAGT CGTCTCAAGA AACTATCAAA AGGAAACAAA 960

GAAAAGGTTC AACTGATTTT GGTTATGAGC CGTGATGCTC GTCTCTATGT TTTGGACGAA 1020

CCCATTGGTG GGGTGGATCC AGCAGCCCGT GCTTATATCC TCAATACCAT TATCAACAAC 1080

TACTCACCAA CTTCTACCGT TTTGATTTCT ACCCACTTGA TTTCTGATAT CGAGCCAATC 1140

TTGGATGAAA TTGTCTTCCT AAAAGACGGA AAAGTCGTCC GTCAAGGAAA TGTAGATGAT 1200

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CAAAGGAGAT TATTTATGTT TTGGAATTTA GTTCGCTACG AATTTAAAAA TGTTAACAAG 1320

TGGTATTTAG CCCTCTACGC AGCCGTGCTA GTCCTTTCTG CCCTCATCGG AATACAGACA 1380

CAAGGCTTTA AAAATCTACC TTACCAAGAA AGTCAGGCTA CTATGCTACT TTTTCTAGCT 1440

ACAGTCTTTG GTGGCTTGAT GCTTACACTT GGGATTTCAA CCATTTTCTT GATTATTAAA 1500

CGCTTCAAAG GTAGTGTCTA CGACCGACAA GGCTATCTGA CTTTGACCTT GCCAGTTTCT 1560

GAACACCATA TCATCACAGC CAAACTAATC GGTGCCTTTA TCTGGTCATT GATTAGCACC 1620

GCTGTATTGG CTCTAAGTGC TGTTATTATT CTGGCTTTAA CAGCTCCAGA ATGGATTCCT 1680

CTTTCTTATG TGATTACATT TGTAGAAACA CATCTCCCTC AGATCTTTCT TACAGGTATA 1740

TCCTTCCTAC TAAATACTAT TTCAGGAATC CTCTGCATCT ACCTGGCTAT TTCCATTGGA 1800

CAGCTTTTCA ATGAATACCG TACAGCACTC GCTGTTGCAG TCTACATTGG TATCCAAATC 1860

GTCATTGGAT TTATTGAACT TTTCTTCAAT CTTAGTTCTA ATTTCTATGT CAATTCACTG 1920

GTAGGACTCA ATGACCATTT CTATATGGGA GCAGGTATAG CCATTGTTGA AGAACTCATA 1980

TTCATAGCTA TCTTTTATCT CGGAACCTAC TACATCTTGA GAAATAAGGT TAATTTGCTT 2040

TAAATAATTT TTACCTAGAT ATGTAACATA CTCATAGAAC AAAAGAGACC AGGCAAAAAG 2100

TCTTTAAAAT TAGAAAACGC ATAGTATCAG GTGTTGAATA TGTACTGCcC CCCAAAAGTT 2160

AGATTTTTTC TGTCTAACTT TTGGGGGCAG TTCATAAGAA CCTTGGTAAT ATGCGTTTTT 2220

320

TGTGAGCTGA CTTATTTCCT TTCACTATAT CGCAAAATGA AATAAGAACG GAACGATGGG 2280

ATTTTGGAAT TCAAATCAAT TTATAAGAAT GTTTTAGAAG TAATATTATC CTATTCCAGA 2340

TTCAGTTCAC TATACAATTG AGTTTTCAAG CAACCTGTTT ACATAATGTG TACATAATTA 2400

GGTTCGTGAT TCCACCCTTT TCACCTTTAA AAACCTCGCT TTCGCAAGGC TCTTCTATTT 2460

ATAAGATAAG GCACGTTTAA AGGTTTTCCA AATCCCTAAA TCATCCGTTT GAAGAACGAG 2520

ACTAGCATAC ATGCGTCCGA TAAATCCTGT TGCTACCACC GCAAAAATCA CTGTAATAGC 2580

AAGTGAAATC CATGCTTCTG CTCCCCCCGC ATAGTCATTA ATCGTTCGAA ACGGCATAAA 2640

GAAGGTCGAA ATAAAGGGAA TATAAGAACC AATCTTCAAG AGGAGATTGT CACCAGCTGC 2700

ACCTAGAGCT GTCACTCCAA AAAAACCACC CATAATCAAA ATCATCAAAG GCGACAAGGC 2760

TTTCCCTGAG TCCTCAGGAC GAGAAACCAT AGATCCTAGG AAGGCTGCCA AGACTACGTA 2820

CATGAAAAGA CTGATCAAAA TAAAGAGCAA GGTATTCAGT GAGATAGCAT CTCCCAAGTG 2880

ATCCAAAATA CCAGACTGAG CCAAGAATGG CAAATCTTTA AAGAGCAAAA CGGCAGCCAG 2940

ACCACCTACA ACATAGATCC CAATATGCGT TAAAATCACT AGAAACAGAG CCATCATCCG 3000

CGCATAGAAA TAGTGACTTG CCCTTATGCT AGAAAAAACG ACTTCCATAA TTTTGGTGCC 3060

TTTTTCACTG GCAACTTCCT GAGCTGTTAC ACCCGCATAG GTAATCAGAA TCATATAAAG 3120

AAAGAATCCT AAGGCACCTG CTGCAATTGT TTGAATAAAC TTTTTATTTT CCTTGGCTTC 3180

ATCAATCTTT TCTGTGAATT GAATTGTCTG CGCTAAGCGT TTTTCCTGCT CTTGAGACAA 3240

GGAAGCAGTT GAACGATTAA GCTGATTTTG CAGTTCATTG AGTGTACCTG TAACCTCAAA 3300

TTTAATTCCA TTTTCAAGCG ATGTTTCGCC ATGATAAACT GCCTTTAGAA CACTATCTTC 3360

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TTCGTCTTTA TAGTCGAAGT TAACACCATT TACATTCTTC AGTCCTTCTG CTACAGATGG 3480

CACTGTTGTC ACTACTGCCA CTTTATTATT TTTAGCCATA GAAGAACCTT GGAGATGCCC 3540

AATTCCTACA GAGATTCCTA AAAAGAGGAA CGGCGAAATC ACCATAAAGA AGAAACTCCA 3600

TGACTCGACA TGTCGAAGAT AGGTTTCCTT GATTACAACC CACATATTTC TCATACTTCC 3660

ACTCCTGATT CTAGTTTAAA GATTTCATCG ATAGTTGGCG CTTGTTGGTC AAATGTTGCG 3720

ATATATTGAC CTTGAGTCAA GATTGAGAAG AGTTCCCTTC CAGCGCTCTC ATCCTCCAAA 3780

ATCAATTTCC AACTGCCTTG TTTGGTCAAG CTCACCTGTT TGACATGAGG AAGATTTTCC 3840

AATTCTTCCT TGCTTCGTTC ACTTGAAACA AAGAGACGCG TTTTCCCGTA TTGATTGCGG 3900

ACATCCTGAA CTGGTCCGTG CAAGACCACA CGGCCATCTC GGATCATCAG AATATCGTCA 3960

CAAAGTTCCT CAACATTGGT CATGACATGG TCAGAAAAGA TAATGGTTGT CCGCGCTCTT 4020

TTTCCTGAAA AATGACTTGT TTGAGCAATT CTGTATTAAC TGGGTCCAAT CCACTAAAAG 4080

GCTCATCCAA GATAATCAGG TCTGGTTCAT GAATCAGAGT AATAATGAGC TGAATCTTCT 4140

GCTGATTTCC TTTTGACAGA CTCTTGATTT TATCTGTCAG CTTTCCTTTC ACTTCCAACC 4200

TCTTCATCCA TTGAGGGAGT TTTTCTTTGA CTTCTTTGGC ATCCATGCCT TTTAGAGTCG 4260

CCAAGTAGCG AACTTGTTCA AGAACTGTCA ATTTAGGCAT GAGATGCGTT CTTCAGGCAG 4320

ATAACCAATC CGAGCATAGG TCTCCTGACG AATATCCTGA CCATCCAGAC CGATTTCTCC 4380

CTGATATTCT AGGAATTTCA AAATACTATG GAAAATCGTT GTTTTTCCAG CACCATTTTT 4440

TCCGACTAGT CCCAAAATAC GACCTGGTCG CGCTTGAAAG TCAATACCAA ACAAAACTTG 4500

CTTGGATCCA AAACTTTTCT CTAGACTTCT TACTTCTAGC ATCTTTCACC TCCGAAATTT 4560

CTTGCACTCA TTATACTCCT TTTTGATAGC CTTTACAATG TTTTTTGTCC ATTTTTAGAA 4620

GACTATTGCT GTGTAAAATA TGGCCTGGAG CACTTTTATA CTCAATGAAA ATCAAAGAGC 4680

AAACTAGGAA GCTAGCCGTA GACTGCTCAA AGTACAGCTT TGAGGTTGCA GATAAAACTG 4740

ACGAAGTCgA CTCAAAACAC TGTTTTGAGG TTGTGGATAG AACTGACGAA kCrTAaCTAT 4800

ATCTACGGCA AGGCGAAcTG ACGTGGTTTG AAGAGATTTT CGAAGAGTAT TAGTGATAAA 4860

TCCATTATAC AGCAGCAAAC TTAATTTATA CCTTCCGCTC CTCAACTGTC TATTTTTAAT 4920

CCTGAATTGT TATTTGAGTA ACTCCTTTTT CCTCGTAAAG TTTTCTTCCT CTAAAACTTC 4980

TGGAAAAAGG CTAATAGTTT CAGACAACAT TTTTATAAGA AACAAGTTCA TCTGTCATTT 5040

CAAGAAGGAG TAATCCTTTA TCTACTAATG GACGGAACAG AATTCAACCG CTTGTCCGAT 5100

ATGTTTTCTA AGGATTATAT AGTAAAATGA AATAAGAACA GGACAAATTG ATCAGGACAG 5160

TCAAATTGAT TTCTAACAAT GTTTTAGAAG TAGATGTATA CTATTCTAGT TTCAATCTGC 5220

TATATCTATT ATGCACACCC CTATAGGATC TAATGAAAAT CACAACAGGC TCATTCATAG 5280

ATGGTTACCT AAGCCTAAGG GAACTAAGAA AACGACTACC AAGGAAGTCG CATTCATCGA 5340

AAAGTAGATT AACAACTATC CTAAAAAATG CTTGAACTAC AAGTCCCCCA GAGAAGACTT 5400

CTGGATGACT AACTTGAACT TGAAATTTAG CAATAATTAA TTCACTATCT AACTATATTT 5460

AGTAATTATT TCAGAACTGA TTAATATTAA AATTAACTAA CAATTCAAAG GATTCATACT 5520

AGCCATAAAT TACGTCCATC AGAGAGAGAC TCTTACTACT TTTAGATTTT AGTCTTTCTA 5580

GCTTCAGAAT ACATCTAAAC TTTAGGGAAA ATGACTATTC GAAAGCGCGA ATGCCTCAAA 5640

ATTATCTCAG ATAAGCTATT CGAAACTTAG AATGCTTTTA AATTTATGGA ATTGCGATTA 5700

TTCGAAACCT AGAATGCATA TAACCTTTAG TTGACAGACC TATTCTAAGT CTCGAAGGGC 5760

TATTTACTTT CTATTCCTTA TCAAAAAAGA CTCATTCCCC CTTTCTCCTC CAAAATATGG 5820

TATAGTAGAA ATATACTATC TATGAGGAGT TTACATGTCA CAGGATAAAC AAATGAAAGC 5880

TGTTTCTCCC CTTCTGCAGC GAGTTATCAA TATCTCATCG ATTGTCGGTG GGGTTGGGAG 5940

TTTGATTTTC TGTATTTGGG CTTATCAGGC TGGGATTTTA CAATCCAAGG AAACCCTCTC 6000

TGCCTTTATC CAGCAGGCAG GCATCTGGGG TCCACCTCTC TTTATCTTTT TACAGATTTT 6060

ACAGACTGTC GTCCCTATCA TTCCAGGGGC CTTGACCTCG GTGGCTGGGG TCTTTATCTA 6120

CGGGCACATC ATCGGGACTA TCTACAACTA TATCGGCATC GTGATTGGCT GTGCCATTAT 6180

CTTTTATCTA GTGCGCCTAT ACGGAGCTGC CTTTGTCCAG TCTGTCGTCA GCAAGCGCAC 6240

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TTATACCTAC GGTCTGACCT ATATTATTGA CTTTTTCTGG CAAATGCTTT GACACGTAAA 6480

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CCTTTCCGCC GTGATAGAAA CACCTGAAAT CTAATGGTTT CAGGTATTCG GAAACTTTGA 6660

GCCTAGTGTC TCAAAGTTTA GGTATGGAAT TTTGAAGAAA GTCGCTACCG TCCGTAATCA 6720

CTTAAGGAAA GGCTCAAAAA TATTGTTTTC AACCACAAAA TCCGTTTGGT TTCCCAAGCG 6780

GATTTTGTGC TTTATTTTGA AACTTCTTTT GCAAGAACAA AGTTCCCAAG TGTGGCAGAA 6840

CCATTTCCTG CGACTGCTGG CGTCACGATA TAGTCACGCA CATCTGGTAC TGGTAGGTAA 6900

CCATTAAGAA GAGATGTAAA TTTCTCACGG ACACGGTCCA GCATATGTTG TTGAGCCATG 6960

ACCCCTCCAC CAAAGACAAT CACGTCTGGG CGGAAAGTCA CTGTCGCATT AACCGCAGCT 7020

TGAGCGATAT AGTAGGCTTG AACATCCCAA ACAGGGTTGT TGAGTTCAAT AGTTTCCCCA 7080

CGTACACCTG TACGAGCTTC CAAACTTGGA CCAGCTGCAT AACCTTCTAG ACATCCCTTA 7140

TGGAAAGGAC AAACACCCTT AAACTCTTTT TCAATATCCA TTGGGTGTCT AGCAACATAA 7200

TAATGACCCA TTTCAGGGTG ACCCACACCA CCGATAAACT CACCACGTTG GATGACGCCT 7260

GCACCGATAC CTGTACCGAT TGTGTAGTAA ACCAAGTTTT CGATACGACC ACCAGCATTG 7320

TTACGGGCAA CCATTTCACC GTAAGCAGAG CTGTTTACGT CTGTTGTGAA GTACATTGGC 7380

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GTCGTCGTGA TAAAGCCATA AGTTTTTGAG TTTTTGTCAA TATCAATCGG CCCAAATGAA 7500

CCAACTGCAA GACCAGCAAG GTTATCGAAT TTTGAGAAGA ACTCAATGGT TTTATCGATT 7560

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CCGACAGCAC AGACAAACTT TGTACCGCCC GCTTCCAAGC TTCCATATAA TTTTGTCATG 7680

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TTTTTTAGAT TTTCCTCTGT AAATCTTACT ATCTAATAAA AACGAACAAA CATGTCATTT 7800

GTTCGTTTTC ACATTAGAGA GGATTGATTA GATTTTCACT TCGATCACAG CATCCCCCTT 7860

AGCAACTGAA CCTGTTGCGA CTGGAGCTAC TGAAGCGTAG TCACCTGTAT TTGTAACGAT 7920

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AACATCGCCA GCTTTCACCT TATTACCTTG AGCAACTTTT GTTTCAAAAC CGTCACCGTT 8040

CATAGATACA GTATCAATAC CAACATGAAT CAAAACTTCA GCACCATTTC TTGTTTTCAA 8100

ACCAAAAGCG TGCCCTGTTG GAAAGGCAAT TGAAACTTCA GCATCAGCTG GTGCATAGAC 8160

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GTCATTGACA TCAGCAAGAG CGACAACATC ACCGACGATA GGAGTTACAA GTGTTTCATT 8280

TTGAAGAGCT GCTGGCGCAA CTTCTTCTTT TTCTTCAGCC ACTTCAGCTC GTTTTGCAGC 8340

TGCAGTTGCG TCTACTTCAT CTTCGTAACC AAACATGTAA GTAAGAGCAA AACCAAGGGC 8400

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TCCACCACCG ATTGCACCAG CAATCAATGA AAGGAAGAAT GGTTTACGGA AGCGCAAGTT 8580

CACCCCGAAG ATAGCAGGCT CTGTAATACC TAGGAAGGCA GAAAGAGCAG CCGGGAAAGC 8640

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AGCTGTCATA GCAGCTGTGA TGATAGCGTT GAATGGGTTA GCATGGTCAG CAGCAAGTAA 8760

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CCAACGGCAG GATTTCCACC AAATACACGG AAGGTTGACC ACACAACCAA ACCTGGCAAG 9240

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GGGATGATTG GAACGAAAAC ATCACCAAAA GTACGGATAG CACGTTGGAA CCAGTTCCCT 9420

TGTTTAGCAA CTTCTGCTTT CATGTCATCC TTAGATGATG TTGGTAATCC AAGTACAACA 9480

ACTTCATCGT ACATTTTGTT AACTGTACCT GTACCAAAGA TAATTTGGTA TTGCCCTGAG 9540

TTAAAGAAAG CACCTTGAAC TTTTTCCAAG TTCTCAATCA CTTCTTTATT GATTTTCTCT 9600

TCATCTTTGA CCATGACACG TAGACGAGTC GCACAGTGGG CAACACTATT GACATTTTCA 9660

CGTCCGCCCA AGGCATCGAT GACTTTTTTT GCAATTTCCT GATTGTTCAT TTGCAAAAAT 9720

CTCCTTATAT AACATTTTGT TCTTGTTTGA AAGCGATTTT ATTCGCCGG 9769

(2) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3149 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

CGCTTGAGTG CTAATTCATA GTTCTATTGT ATCACTTGGT CAGAAATAAT CAAGAAAAAA 60

GTCTGACTTT CTCAAGATAA AAAGCCTGAG ACCAACTCAG ACTTTTTAAT TCTTAAAATG 120

GCAATTCTTC CTCTTCCAAG ACCAAATCTG CCAAATCTTG GCCTGCATTA TTTTCACGCA 180

TAGCACGTTG GGCACGACTT TCCAAGAGTT GGAATCCTGT GACAAGTACT TCGGTCACGT 240

AGTTCATTTG GCCATTTTTC TCAAAGCGAC GGGTACGCAA TTCTCCATCA ACGGAAATGA 300

GACTACCTTT GGTTGCGTAC TTGCCAAAGT TTCTGCTAGT CTGCCCCATA GGACCATATT 360

GACAAAATCA GCTTCACGTT CACCGTTTTG GTCTTTGTAA CGACGGTTCA CAGCGATAGT 420

TGCTCGCGCT ACCGACTTGT CATTGTTGGT TTTGTGCAAT TCTGGTGTAG ACGTTAAACG 480

TCCAATCAAG ATAACTTTAT TATACATATT TTCTTCCTCC TACTTATCTA TTCGTAGGAA 540

ATCAAAAAAA GTTACAGAAA TTTGTAACTT TTCGAGAAAA TTTTTTATTT TTTATGAACC 600

ATGAAACCTG TCGCCTGTTG ATTGGCCATA ATGGTCATAT CTGTAATCTG AACACGACGA 660

GGTTGACTAG TCACATAGAC TACTGTATCT GCAATATCCT GAGCTTGCAA AGCTTCTATT 720

CCTTGGTAAA CGGACGCAGC TCGTTCTTTA TCACCATGAA AACGCACTGT AGAAAAATCT 780

GTTTCGACAA TTCCAGGCTG AATGGTCGTC ACCTTGATAT CCGTTGCGAT GGTATCAATT 840

CGCAGTCCAT CTGAAAAGGT CTTAACTGCC GCCTTGGTGG CTGAGTAAAC AGCTGCACCA 900

GCATAGGCAT AAATTCCTGC GGTTGACCCC ATATTGATAA TATGACCTTG ATTGGCTTTT 960

What Is Claimed Is:

1. Computer readable medium having recorded thereon the nucleotide sequence depicted in SEQ ID NOS:1-391, a representative fragment thereof or a nucleotide sequence at least 95% identical to a nucleotide sequence depicted in SEQ ID NOS:1-391.

2. Computer readable medium having recorded thereon any one of the fragments of SEQ ID NOS:1-391 depicted in Tables 2 and 3 or a degenerate variant thereof.

3. The computer readable medium of claim 1, wherein said medium is selected from the group consisting of a floppy disc, a hard disc, random access memory (RAM), read only memory (ROM), and CD-ROM.

4. The computer readable medium of claim 3, wherein said medium is selected from the group consisting of a floppy disc, a hard disc, random access memory (RAM), read only memory (ROM), and CD-ROM.

5. A computer-based system for identifying fragments of the *Streptococcus pneumoniae* genome of commercial importance comprising the following elements:

a) a data storage means comprising the nucleotide sequence of SEQ ID NOS:1-391, a representative fragment thereof, or a nucleotide sequence at least 95% identical to a nucleotide sequence of SEQ ID NOS:1-391;

b) search means for comparing a target sequence to the nucleotide sequence of the data storage means of step (a) to identify homologous sequence(s), and

c) retrieval means for obtaining said homologous sequence(s) of step (b).

6. A method for identifying commercially important nucleic acid fragments of the *Streptococcus pneumoniae* genome comprising the step of comparing a database comprising the nucleotide sequences depicted in SEQ ID NOS:1-391, a representative fragment thereof, or a nucleotide sequence at least 95% identical to a nucleotide sequence of SEQ ID NOS:1-391 with a target sequence to obtain a nucleic acid molecule comprised of a complementary nucleotide sequence to said target sequence, wherein said target sequence is not randomly selected.

7. A method for identifying an expression modulating fragment of *Streptococcus pneumoniae* genome comprising the step of comparing a database comprising the nucleotide sequences depicted in SEQ ID NOS:1-391, a representative fragment thereof, or a nucleotide sequence at least 95% identical to the nucleotide sequence of SEQ ID NOS:1-391 with a target sequence to obtain a nucleic acid molecule comprised of a complementary nucleotide sequence to said target sequence, wherein said target sequence comprises sequences known to regulate gene expression.

8. An isolated protein-encoding nucleic acid fragment of the *Streptococcus pneumoniae* genome, wherein said fragment consists of the nucleotide sequence of any one of the fragments of SEQ ID NOS:1-391 depicted in Tables 2 and 3, or a degenerate variant thereof.

9. A vector comprising any one of the fragments of the *Streptococcus pneumoniae* genome SEQ ID NOS:1-391 depicted in Tables 2 and 3 or a degenerate variant thereof.

10. An isolated fragment of the *Streptococcus pneumoniae* genome, wherein said fragment modulates the expression of an operably linked open reading frame, wherein said fragment consists of the nucleotide sequence from about 10 to 200 bases in length which is 5' to any one of the open reading frames depicted in Tables 2 and 3 or a degenerate variant thereof.

11. A vector comprising any one of the fragments of the *Streptococcus pneumoniae* genome of claim 8.

12. An organism which has been altered to contain any one of the fragments of the *Streptococcus pneumoniae* genome of claim 8.

13. An organism which has been altered to contain any one of the fragments of the *Streptococcus pneumoniae* genome of claim 10.

14. A method for regulating the expression of a nucleic acid molecule comprising the step of covalently attaching to said nucleic acid molecule a nucleic acid molecule consisting of the nucleotide sequence from about 10 to 100 bases 5' to any one of the fragments of the *Streptococcus pneumoniae* genome depicted in SEQ ID NOS:1-391 and Tables 2 and 3 or a degenerate variant thereof.

15. An isolated nucleic acid molecule encoding a homolog of any of the fragments of the *Streptococcus pneumoniae* genome of SEQ ID NOS:1-391 and Tables 2 and 3, wherein said nucleic acid molecule is produced by a process comprising steps of:

a) screening a genomic DNA library using as a probe a target sequence defined by any of SEQ ID NOS:1-391 and Tables 2 and 3, including fragments thereof;

b) identifying members of said library which contain sequences that hybridize to said target sequence; and

c) isolating the nucleic acid molecules from said members identified in step (b).

16. An isolated DNA molecule encoding a homolog of any one of the fragments of the *Streptococcus pneumoniae* genome of SEQ ID NOS:1-391 and Tables 2 and 3, wherein said nucleic acid molecule is produced a process comprising steps of:

a) isolating mRNA, DNA, or cDNA produced from an organism;

b) amplifying nucleic acid molecules whose nucleotide sequence is homologous to amplification primers derived from said fragment of said *Streptococcus pneumoniae* genome to prime said amplification;

c) isolating said amplified sequences produced in step (b).

17. An isolated polypeptide encoded by any of the fragments of the *Streptococcus pneumoniae* genome of SEQ ID NOS:1-391 and depicted in Table 2 and 3 or by a degenerate variant of said fragments.

18. An isolated polynucleotide molecule encoding any one of the polypeptides of claim 17.

19. An antibody which selectively binds to any one of the polypeptides of claim 17.

20. A method for producing a polypeptide in a host cell comprising the steps of:

a) incubating a host containing a heterologous nucleic acid molecule whose nucleotide sequence consists of any one of the fragments of the *Streptococcus pneumoniae* genome of SEQ ID NOS:1-391 and depicted in Tables 2 and 3, under conditions where said heterologous nucleic acid molecule is expressed to produce said protein, and

b) isolating said protein.

Figure 1

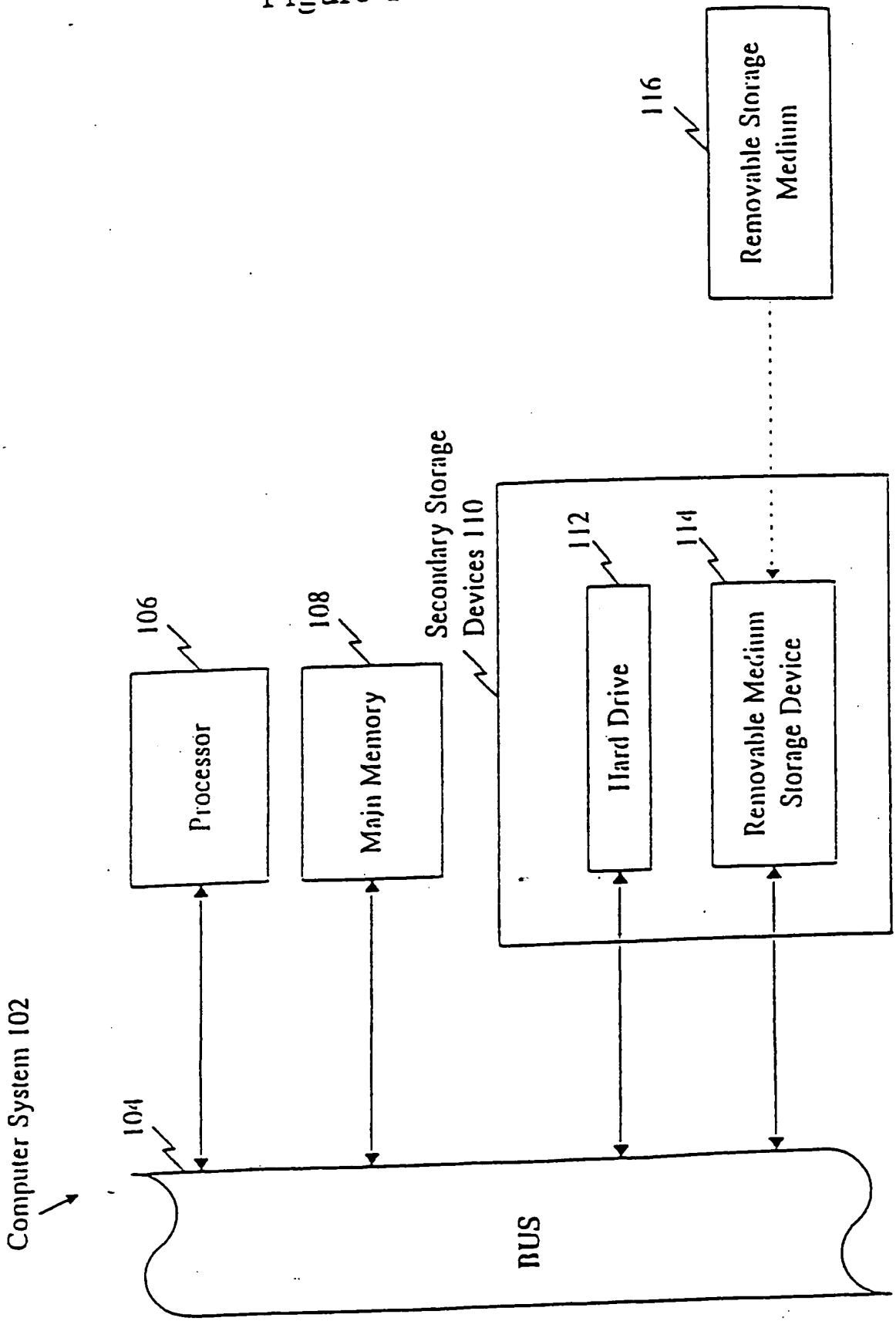
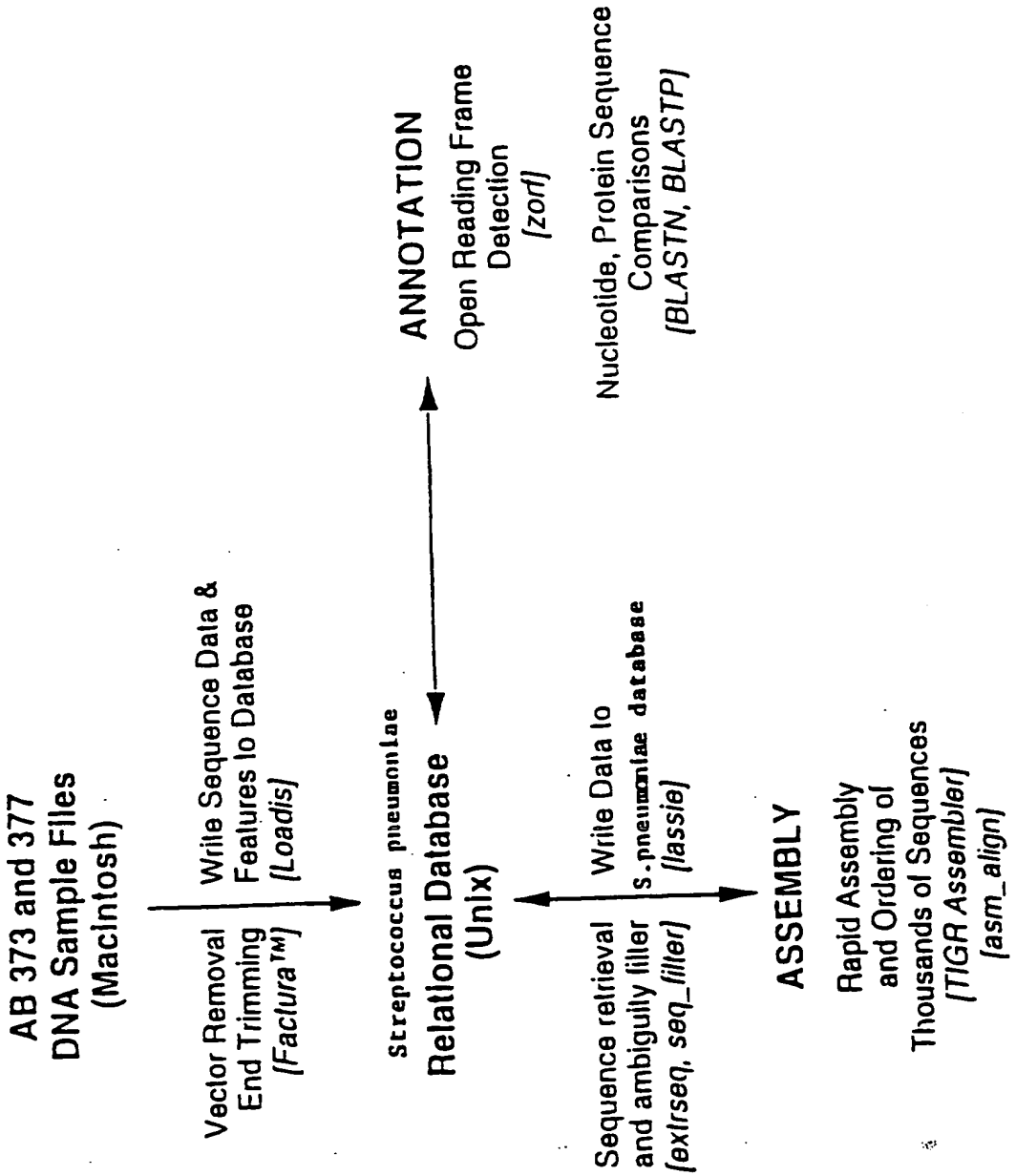

116
Removable Storage Medium
Secondary Storage Devices 110
112
Hard Drive
114
Removable Medium Storage Device
106
Processor
108
Main Memory
Computer System 102
104
BUS

Figure 2


AB 373 and 377
DNA Sample Files
(Macintosh)
Vector Removal
End Trimming
(Factura™)
Write Sequence Data &
Features to Database
(Loadis)
Streptococcus pneumoniae
Relational Database
(Unix)
ANNOTATION
Open Reading Frame
Detection
(zorf)
Nucleotide, Protein Sequence
Comparisons
(BLASTN, BLASTP)
Sequence retrieval
and ambiguity filler
(extrseq, seq_filler)
Write Data to
S.pneumoniae database
(lassie)
ASSEMBLY
Rapid Assembly
and Ordering of
Thousands of Sequences
(TIGR Assembler)
(asm_align)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 97/19588

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/31 C07K14/315 C07K16/12 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 33276 A (HUMAN GENOME SCIENCES INC ;UNIV JOHNS HOPKINS (US)) 24 October 1996 see claims 1-7 ---	1-7
A	ALTSCHUL S F ET AL: "BASIL LOCAL ALIGNMENT SEARCH TOOL" JOURNAL OF MOLECULAR BIOLOGY, vol. 215, 1990, pages 403-410, XP000604562 cited in the application see the whole document ---	1-7

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 March 1998	08.07.98
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer HORNIG H.

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	W.R. PEARSON AND D.J. LIPMAN: "Improved tools for biological sequence comparison" PROC. NATL. ACAD. SCI., vol. 85, April 1988, NATL. ACAD. SCI.,WASHINGTON,DC,US;, pages 2444-2448, XP002060460 cited in the application see the whole document	1-7
A	WO 95 06732 A (UNIV ROCKEFELLER ;MASURE H ROBERT (US); PEARCE BARBARA J (US); TUO) 9 March 1995 see the whole document	1-7
A	WO 95 31548 A (UAB RESEARCH FOUNDATION ;YOTHER JANET (US); DILLARD JOSEPH P (US)) 23 November 1995 see the whole document	1-7
A	WO 95 14712 A (RES CORP TECHNOLOGIES INC) 1 June 1995 see the whole document	1-7
A	WO 96 05859 A (AMERICAN CYANAMID CO) 29 February 1996 see the whole document	1-7
A	WO 93 10238 A (US HEALTH) 27 May 1993 see the whole document	1-7
A	EP 0 687 688 A (UNIV OVIEDO ;UNIV LEICESTER (GB)) 20 December 1995 see the whole document	1-7
A	EP 0 622 081 A (UAB RESEARCH FOUNDATION) 2 November 1994 see the whole document	1-7

INTERNATIONAL SEARCH REPORT

...ernational application No.
PCT/US 97/ 19588

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 1-4 could be, at least partially be considered as a mere presentation of information Rule 39.1(v), and claims 5-7 at least partially as a computer program, Rule 39.1(vi)PCT, the search has been carried out as far as possible in our systematic documentation.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see continuation-sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-7

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-7

Computer readable medium having recorded thereon the nucleotide sequence depicted in SEQ ID nos. 1-391, a representative fragment thereof or a nucleotide sequence at least 95% identical to a nucleotide sequence depicted in SEQ ID nos. 1-391; a computer-based system for identifying fragments of the Streptococcus pneumoniae genome of commercial importance comprising: a) a data storage means comprising said nucleotide sequence(s); b) search means for comparing a target sequence to the nucleotide sequence of the data storage means of step (a) to identify homologous sequence(s), and c) retrieval means for obtaining said homologous sequence(s) of step (b); a method for identifying commercially important nucleic acid fragments of the Streptococcus pneumoniae genome comprising the step of comparing a database comprising said nucleotide sequence(s) with a target sequence to obtain a nucleic acid molecule comprised of a complementary nucleotide sequence to said target sequence, wherein said target sequence is not randomly selected; a method for identifying an expression modulating fragments of the Streptococcus pneumoniae genome comprising the step of comparing a database comprising said nucleotide sequence(s) with a target sequence to obtain a nucleic acid molecule comprised of a complementary nucleotide sequence to said target sequence, wherein said target sequence comprises sequences known to regulate gene expression;

2. Claims: (8-20) partially

An isolated protein-encoded nucleic acid fragment of the Streptococcus pneumoniae genome, wherein said fragment consists of the nucleotide sequence of the fragment of SEQ ID no.1 depicted in Tables 2 and 3, or a degenerate variant thereof; a vector comprising the fragment of the Streptococcus pneumoniae genome SEQ ID no.1; an isolated fragment of the Streptococcus pneumoniae genome, wherein said fragment modulates the expression of an operably linked open reading frame, wherein said fragment consists of the nucleotide sequence from about 10 to 200 bases in length which is 5' to any one of the open reading frame of SEQ ID no.1 depicted in Tables 2 and 3 or a degenerate variant thereof; a method for regulating the expression of a nucleic acid molecule comprising the step of covalently attaching to said nucleic acid molecule a nucleic acid molecule consisting of the nucleotide sequence from about 10 to 100 bases 5' to any one of the open reading frame of SEQ ID no.1 and Tables 2 and 3 or a degenerate variant thereof; an isolated nucleic acid molecule encoding a homolog of SEQ ID no.1; an isolated polypeptide encoded by SEQ ID no.1 and depicted in Table 2 and 3; an antibody which selectively binds to any one of said polypeptides, a method for producing a polypeptide in a host cell comprising a) incubating a host containing a heterologous nucleic acid

molecule whose nucleotide sequence consists of SEQ ID no.1 and depicted in Table 2 and 3, under conditions where said heterologous nucleic acid molecule is expressed to produce said protein, and b) isolating said protein;

3-392. Claims:(8-20) partially

Idem as subject 2 but limited to each of the sequences of SEQ ID no. 2 to 391;

For the sake of conciseness, the second subject matter is explicitly defined, the other subject matters are defined by analogy hereto.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 97/19588

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9633276 A	24-10-96	AU 5552396 A	07-11-96
		EP 0821737 A	04-02-98
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		CA 2170726 A	09-03-95
		EP 0721506 A	17-07-96
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		CA 2198251 A	29-02-96
		EP 0778781 A	18-06-97
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		ES 2088820 A	16-09-96
		WO 9516711 A	22-06-95
EP 0622081 A	02-11-94	AU 682018 B	18-09-97
		AU 5769694 A	27-10-94
		CA 2116261 A	21-10-94
		FI 941695 A	21-10-94
		JP 7126291 A	16-05-95
		NO 941420 A	21-10-94
		US 5679768 A	21-10-97
		ZA 9401584 A	12-10-94